

L56 15 SEA FILE=ZCAPLUS ABB=ON PLU=ON L51
 L60 31 SEA FILE=ZCAPLUS ABB=ON PLU=ON L39 OR L36 OR (L54 OR L55 OR L56)
 L62 1 SEA FILE=REGISTRY ABB=ON PLU=ON THIONYL CHLORIDE/CN
 L63 4 SEA FILE=ZCAPLUS ABB=ON PLU=ON L62 AND L60
 L64 1 SEA FILE=REGISTRY ABB=ON PLU=ON METHANOL/CN
 L65 7 SEA FILE=ZCAPLUS ABB=ON PLU=ON L64 AND L60
 L66 8 SEA FILE=ZCAPLUS ABB=ON PLU=ON L63 OR L65

=> d ibib abs hitind L66 1-8

L66 ANSWER 1 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:327700 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:337872

TITLE: Process for preparation of methyl (+)-(S)- α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetate (clopidogrel) via cyclocondensation of methyl (+)- α -(2-thienylethylamino)-N-(2-chlorophenyl)acetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid.

INVENTOR(S): Srivastava, Anita Ranjan; Pawar, Prashant Pandurang; Poojari, Krishna Anand; Patil, Pravin Chaitram; Dalvi, Rajiv Ramchandra

PATENT ASSIGNEE(S): RPG Life Sciences Limited, India

SOURCE: PCT Int. Appl., 24pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

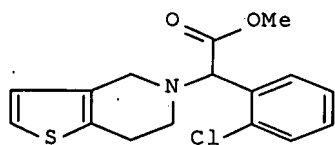
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007032023	A2	20070322	WO 2006-IN250	20060707
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

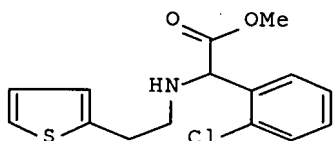
PRIORITY APPLN. INFO.: IN 2005-MU836 A 20050709

OTHER SOURCE(S): CASREACT 146:337872

GI



I



II

- AB A process for preparation of clopidogrel (I) comprises reaction of Me (S)- α -(2-thienylethylamino)-N-(2-chlorophenyl)acetate (II) salt with H₂CO in H₂O in the presence of catalytic hydrochloric acid under heating followed by separation of the aqueous layer from the sticky mass, extraction of the aqueous layer with petroleum ether or hexane at pH 2-3, and concentration of the organic layer. Thus, II.HCl, H₂CO, and cat. HCl were heated together in H₂O at 78-80° for 2 h; the aqueous layer was separated and extracted twice with petroleum ether to give after concentration 83.57% I of 99.90% purity.
- CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45
- IT **113665-84-2P**, Clopidogrel
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation clopidogrel via cyclocondensation of Me thienylethylaminochlorophenylacetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid)
- IT **120202-66-6P**, Clopidogrel hydrogen sulfate
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(preparation clopidogrel via cyclocondensation of Me thienylethylaminochlorophenylacetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid)
- IT **67-56-1**, Methanol, uses 67-63-0, Isopropyl alcohol, uses 67-64-1, Acetone, uses 78-93-3, Methyl ethyl ketone, uses 108-20-3, Isopropyl ether 108-88-3, Toluene, uses 141-78-6, Ethyl acetate, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation clopidogrel via cyclocondensation of Me thienylethylaminochlorophenylacetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid)
- IT 7664-41-7, Ammonia, reactions **7664-93-9**, Sulfuric acid, reactions
RL: **RGT (Reagent); RACT (Reactant or reagent)**
(preparation clopidogrel via cyclocondensation of Me thienylethylaminochlorophenylacetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid)

L66 ANSWER 2 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:281991 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:337870

TITLE: Process for preparation of clopidogrel and analogues

INVENTOR(S): Wang, Lixin; Tang, Yi; Cheng, Yi; Tian, Fang

PATENT ASSIGNEE(S): Zhejiang Huahai Pharmaceutical Co., Ltd., Peop. Rep. China; Chengdu Organic Chemicals Co., Ltd., Chinese Academy of Sciences

SOURCE: PCT Int. Appl., 73pp.

CODEN: PIXXD2

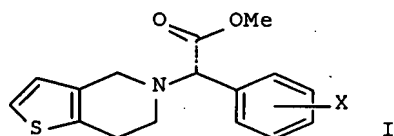
DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007028337	A1	20070315	WO 2006-CN2316	20060907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CN 1927863	A	20070314	CN 2005-10060719	20050908
CN 1927864	A	20070314	CN 2005-10060720	20050908
CN 1927865	A	20070314	CN 2005-10060721	20050908
CN 1927866	A	20070314	CN 2005-10060722	20050908
CN 1951940	A	20070425	CN 2005-10061230	20051021
CN 1951941	A	20070425	CN 2005-10061231	20051021
PRIORITY APPLN. INFO.:				
			CN 2005-10060719	A 20050908
			CN 2005-10060720	A 20050908
			CN 2005-10060721	A 20050908
			CN 2005-10060722	A 20050908
			CN 2005-10061230	A 20051021
			CN 2005-10061231	A 20051021

OTHER SOURCE(S): MARPAT 146:337870
GI



AB This invention provides a process for preparing optically active clopidogrel and its analogs I [wherein X = H, F, Cl, Br, or I] comprising kinetic resolution of racemates. For example, racemic 2-chlorophenyl-(6,7-dihydro-4H-thieno[3,2-c]pyrid-5-yl)acetonitrile (preparation given) was methylated with di-Me sulfate in the presence of potassium hydroxide and triethylbenzylammonium chloride to give racemic clopidogrel. The obtained racemic clopidogrel was reacted with D-camphorsulfonic acid to give (S)-clopidogrel salt with high purity. The (R)-clopidogrel can be recycled by racemization in aqueous solution in the presence of base and phase transfer catalyst.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 113665-84-2P 120202-65-5P 120202-66-6P 120202-67-7P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**

(Preparation)

(preparation of clopidogrel and analogs)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 67-64-1, 2-Propanone, uses 67-66-3, uses 67-68-5, uses 68-12-2, uses 71-36-3, 1-Butanol, uses 75-05-8, Acetonitrile, uses 75-09-2, uses 78-93-3, 2-Butanone, uses 108-10-1 108-88-3, uses 108-90-7, uses 109-99-9, uses 110-71-4 123-86-4 123-91-1, Dioxane, uses 141-78-6, Acetic acid ethyl ester, uses 617-84-5, Diethyl formamide 1300-21-6 1330-20-7, uses 7732-18-5, Water, uses 25321-22-6

RL: NUU (Other use, unclassified); USES (Uses)

(preparation of clopidogrel and analogs)

IT 7647-01-0, Hydrochloric acid, reactions 7664-93-9, Sulfuric acid, reactions 10035-10-6, Hydrobromic acid, reactions

RL: **RCT (Reactant); RGT (Reagent); RACT (Reactant or reagent)**

(preparation of clopidogrel and analogs)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 3 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1354002 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:100660

TITLE: Process for preparation of clopidogrel and intermediates used herein

INVENTOR(S): Kim, Eun Sook; Kim, Hee Cheol; Kwon, Bo Sung; Yun, Sangmin; Ko, Mi Young; Kim, Cheol Kyung; Suh, Kwee Hyun

PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 25pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137628	A1	20061228	WO 2005-KR4017	20051128
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: KR 2005-54303 A 20050623

OTHER SOURCE(S): MARPAT 146:100660

AB This invention provides a process for the preparation of clopidogrel and intermediates used herein, which comprises optically resolving racemic α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid (preparation given) using chiral amines followed by methylation. The process has the advantages of high purity and high yield.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45

IT 75-75-2, Methanesulfonic acid 104-15-4, 4-Methylbenzenesulfonic acid, uses 7647-01-0, Hydrochloric acid, uses **7664-93-9**, Sulfuric acid, uses
 RL: CAT (Catalyst use); USES (Uses)
 (preparation of clopidogrel and intermediates used herein)

IT 716-61-0P **113665-84-2P**, Clopidogrel
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and intermediates used herein)

IT **120202-66-6P**, Clopidogrel hydrogen sulfate 868560-74-1P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
 (preparation of clopidogrel and intermediates used herein)

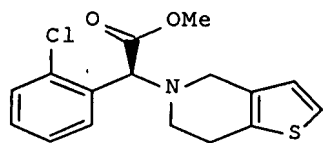
IT **67-56-1**, Methanol, reactions
 RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
 (preparation of clopidogrel and intermediates used herein)

IT 75-44-5, Phosgene 79-22-1, Methyl chloroformate 79-37-8, Oxalyl chloride 81-04-9, 1,5-Naphthalenedisulfonic acid 108-23-6, Isopropyl chloroformate 109-61-5, Propyl chloroformate 299-42-3, Ephedrine 488-43-7, Glucamine 503-38-8, Diphosgene 541-41-3, Ethyl chloroformate 543-27-1, Isobutyl chloroformate **7719-09-7**, Thionyl chloride 10025-87-3, Phosphoryl chloride 10026-13-8, Phosphorus pentachloride 28783-41-7 29270-30-2 32315-10-9, Triphosgene 46032-98-8 54903-50-3 855595-16-3 917613-70-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of clopidogrel and intermediates used herein)

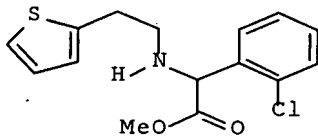
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 4 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:838194 ZCAPLUS Full-text
 DOCUMENT NUMBER: 146:441665
 TITLE: Preparation of clopidogrel
 INVENTOR(S): Bhushan, Lohray Vidya; Bhushan, Lohray Braj; Bipin, Pandey
 PATENT ASSIGNEE(S): Zydus Research Center, Cadila Health Care Ltd., India
 SOURCE: Indian, 33pp.
 CODEN: INXXAP
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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IN 193668	A1	20040731	IN 2001-MU335	20010411
IN 2003MU01007	A	20050715	IN 2003-MU1007	20030924
IN 2003MU01008	A	20050715	IN 2003-MU1008	20030924
PRIORITY APPLN. INFO.:			IN 2001-MU335	A3 20010411
GI				



I



II

- AB A process for the preparation of title compound I and its pharmaceutically acceptable salts was disclosed. For example, 1,3-dioxalane/HCL mediated cyclization of amine II hydrochloride afforded the racemate of clopidogrel in 95% yield.
- IC ICM A61K031-44
ICS C07D495-04
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- IT **90055-48-4P 113665-84-2P, S-Clopidogrel**
120202-66-6P 120202-69-9P 120202-71-3P
135046-48-9P 934504-75-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**;
USES (Uses)
(preparation of clopidogrel)
- IT **67-56-1**, Methanol, reactions 937-14-4, Mcpba 1333-74-0, Hydrogen, reactions 1504-71-8 4648-54-8, Trimethylsilyl azide **7664-93-9**, Sulfuric acid, reactions **7719-09-7**, Thionyl chloride 20762-60-1, Potassium azide 26628-22-8, Sodium azide 40412-06-4, 2-Thiophene ethanol tosylate 934504-65-1
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(preparation of clopidogrel)
- IT 3380-96-9P **141109-13-9P 141109-14-0P**
141109-16-2P 934504-66-2P 934504-67-3P 934504-68-4P
934504-72-0P 934504-73-1P 934504-74-2P
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation of clopidogrel)

L66 ANSWER.5 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:504896 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:83300
TITLE: Process for preparation of clopidogrel and its salt
INVENTOR(S): Mao, Haifang; Pan, Xianhua; Lu, Jiaqing
PATENT ASSIGNEE(S): Shanghai Institute of Technology, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1775782	A	20060524	CN 2005-10111562	20051215
PRIORITY APPLN. INFO.:			CN 2005-10111562	20051215

- AB The title preparation includes esterifying (R)-2-bromo-2-(2-chlorophenyl)acetic acid with methanol in the presence of sulfuric acid or

thionyl chloride to generate Me (R)-2-bromo-2-(2-chlorophenyl)acetate; and reacting Me (R)-2-bromo-2-(2-chlorophenyl)acetate with 4,5,6,7-tetrahydrothieno[3,2- c]pyridine in the presence of base to generate the target product. Further neutralization of the product using an acid can result in corresponding salt.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 IT 7664-93-9, Sulfuric acid, reactions
 RL: CAT (Catalyst use); **RCT (Reactant); RACT (Reactant or reagent);** USES (Uses)
 (preparation of clopidogrel and its salt)
 IT 113665-84-2P 622835-93-2P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and its salt)
 IT 120202-65-5P 120202-66-6P 862163-72-2P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
 (preparation of clopidogrel and its salt)
 IT 67-56-1, Methanol, reactions
 RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
 (preparation of clopidogrel and its salt)
 IT 110-86-1, Pyridine, reactions 121-44-8, Triethyl amine, reactions 144-55-8, Sodium bicarbonate, reactions 497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 7719-09-7, Thionyl chloride
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (preparation of clopidogrel and its salt)

L66 ANSWER 6 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:780708 ZCAPLUS Full-text
 DOCUMENT NUMBER: 141:282821
 TITLE: Process for the preparation of amorphous clopidogrel hydrogensulfate
 INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari
 PATENT ASSIGNEE(S): Hetero Drugs Limited, India
 SOURCE: PCT Int. Appl., 10 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004081015	A1	20040923	WO 2003-IN50	20030310
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003216707	A1	20040930	AU 2003-216707	20030310
IN 2003CN00583	A	20050415	IN 2003-CN583	20030421
US 2006100231	A1	20060511	US 2003-433210	20030530

PRIORITY APPLN. INFO.:

WO 2003-IN50

A 20030310

AB A process for preparation of amorphous clopidogrel hydrogensulfate comprises:
(A) dissolving clopidogrel in methanol, ethanol, or their mixts.; (B) adding concentrated sulfuric acid at approx. 0-50°; (C) refluxing the mixture for approx. 2 h; and (D) removing the solvent from the solution either by distillation, vacuum drying, or by spray drying.

IC ICM C07D495-04

ICS A61K031-44

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 28, 75

IT 120202-66-6P, Clopidogrel hydrogen sulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(process for the preparation of amorphous clopidogrel hydrogensulfate)

IT 113665-84-2, Clopidogrel

RL: RCT (Reactant); RACT (Reactant or reagent)

(process for the preparation of amorphous clopidogrel hydrogensulfate)

IT 7664-93-9, Sulfuric acid, reactions

RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**

(process for the preparation of amorphous clopidogrel hydrogensulfate using)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses

RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)

(solvent; process for the preparation of amorphous clopidogrel hydrogensulfate using)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 7 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:310878 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:287712

TITLE: Racemization of optically active 2-substituted phenylglycine esters

INVENTOR(S): Maheshwari, Krishna K.; Sarma, Rayaprolu Kodandarama; Joshi, Shreerang Vidyadhar; Barde, Anup Ramkrishna; Sutar, Rajiv Pandurang; Ranade, Prasad Vasudeo

PATENT ASSIGNEE(S): USV Limited, India

SOURCE: U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004073057	A1	20040415	US 2002-271299	20021015
US 6812363	B2	20041102		
GB 2394473	A	20040428	GB 2003-24166	20031015
GB 2394473	B	20060315		
DE 10348674	A1	20040527	DE 2003-10348674	20031015
FR 2847579	A1	20040528	FR 2003-12059	20031015

PRIORITY APPLN. INFO.:

US 2002-271299

A 20021015

AB A process for preparing a racemic mixture containing nearly equal amts. of stereo isomers of (2-chlorophenyl)glycine Me ester (I) involves heating an enantiomerically-enriched material with thionyl chloride. A useful enantiomer may thereby be recovered from unwanted mother liquors that would otherwise be discarded. In an example, 73.7 kg thionyl chloride was added to 100 kg (-)-I

in 350 L methanol with stirring at 25-30°, the solution heated at reflux for about 12 h, and water added. Racemic I found in the organic layer was resolved, e.g., by the tartrate method.

IC ICM C07C229-38

INCL 560038000; 562401000

CC 34-2 (Amino Acids, Peptides, and Proteins)

IT 141109-14-0P

RL: PUR (Purification or recovery); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT 141109-16-2P 212838-70-5P

RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation);
RACT (Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT 141109-13-9P 676132-76-6P 676132-77-7P
676132-78-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT 7719-09-7, Thionyl chloride

RL: RGT (Reagent); RACT (Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT 141109-17-3P 213018-92-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD.. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 8 OF 8 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:473265 ZCAPLUS Full-text

DOCUMENT NUMBER: 139:41853

TITLE: preparation of crystal and amorphous forms of
clopidogrel hydrogen sulfate for pharmaceuticals

INVENTOR(S): Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wizel,
Shlomit; Maydan, Sharon Avhar; Lidor-Hadas, Rami

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel

SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003114479	A1	20030619	US 2002-74409	20020212
US 6767913	B2	20040727		
CA 2470479	A1	20030626	CA 2002-2470479	20021218
WO 2003051362	A2	20030626	WO 2002-US40679	20021218
WO 2003051362	A3	20030807		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002366383	A1	20030630	AU 2002-366383	20021218
EP 1467735	A2	20041020	EP 2002-805215	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 200402485	A2	20050428	HU 2004-2485	20021218
JP 2005514387	T	20050519	JP 2003-552295	20021218
CN 1620293	A	20050525	CN 2002-828204	20021218
CN 1923835	A	20070307	CN 2006-10139532	20021218
US 2003225129	A1	20031204	US 2003-339008	20030108
US 7074928	B2	20060711		
ZA 2004004733	A	20050615	ZA 2004-4733	20040615
NO 2004003038	A	20040909	NO 2004-3038	20040716

PRIORITY APPLN. INFO.:

US 2001-342440P	P	20011218
US 2001-342351P	P	20011221
US 2002-348182P	P	20020111
US 2002-74409	A	20020212
US 2002-359157P	P	20020221
CN 2002-828204	A3	20021218
WO 2002-US40679	W	20021218

AB The present invention provides new crystalline forms III, IV and V of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns., and method of treatments with such compns. The present invention further provides a novel process where the amorphous form is converted to Form I by contacting Form I with an ether. Clopidogrel hydrogen sulfate (2 g) was dissolved in MeOH (4 mL). The resulting solution was added dropwise to di-Et ether (350 mL). The suspension was stirred at room temperature for 45 min. The solid was filtered and dried at about 50° in a vacuum oven for 24 h to give 1.12 g (56%) of clopidogrel hydrogen sulfate, which characterization data showed to be the amorphous form.

IC ICM C07D498-02
ICS A61K031-4743

INCL 514301000; 546114000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 28, 75

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 71-23-8, 1-Propanol, uses 71-36-3, 1-Butanol, uses 71-43-2, Benzene, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 78-92-2, 2-Butanol 78-93-3, Methyl ethyl ketone, uses 108-88-3, Toluene, uses 123-91-1, 1,4-Dioxane, uses 141-78-6, Ethyl acetate, uses 1330-20-7, Xylene, uses 1634-04-4, tert-Butyl methyl ether

RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)

(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 120202-66-6P, Clopidogrel hydrogen sulfate,

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 7664-93-9, Sulfuric acid, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 113665-84-2, Clopidogrel

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
(Reactant or reagent); USES (Uses)

(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate
for pharmaceuticals)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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chain nodes :
7 9 10 11 12 14 15 16 17 18
ring nodes :
1 2 3 4 5 6
ring/chain nodes :
8
chain bonds :
1-15 2-16 3-17 4-11 5-7 6-14 7-8 7-9 7-18 9-10 9-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
7-8 9-10 9-12
exact bonds :
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normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

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L42          426 SEA FILE=REGISTRY SSS FUL L40
L43          41 SEA FILE=CASREACT ABB=ON PLU=ON L42
L45          3 SEA FILE=CASREACT SUB=L43 SSS FUL L31 ( 7 REACTIONS)

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100.0% DONE      66 VERIFIED      7 HIT RXNS      3 DOCS
SEARCH TIME: 00.00.01

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FILE 'CASREACT' ENTERED AT 14:28:23 ON 22 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE 'ZCAPLUS' ENTERED AT 14:28:23 ON 22 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L45
PROCESSING COMPLETED FOR L60

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L61          31 DUP REM L45 L60 (3 DUPLICATES REMOVED)
              ANSWERS '1-3' FROM FILE CASREACT
              ANSWERS '4-31' FROM FILE ZCAPLUS

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L61 ANSWER 1 OF 31 CASREACT COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 142:56276 CASREACT Full-text
TITLE: A process for preparation of clopidogrel via
        resolution of methyl  $\alpha$ -[[2-(thien-2-

```

yl)ethyl]amino]- α -(2-chlorophenyl)acetate,
 racemization of the undesired enantiomer, and
 cyclocondensation with formaldehyde

INVENTOR(S): Vaghela, Mukesh Nathalal; Rehani, Rajeev Budhdev;
 Thennati, Rajamannar

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108665	A2	20041216	WO 2004-IN106	20040419
WO 2004108665	A3	20050324		

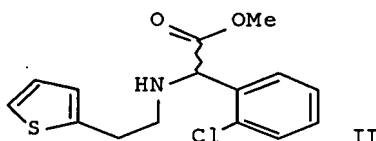
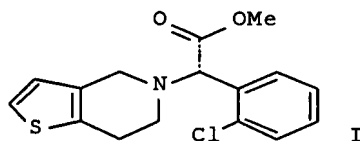
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2003MU00407 A 20050211 IN 2003-MU407 20030424

PRIORITY APPLN. INFO.: IN 2003-MU407 20030424

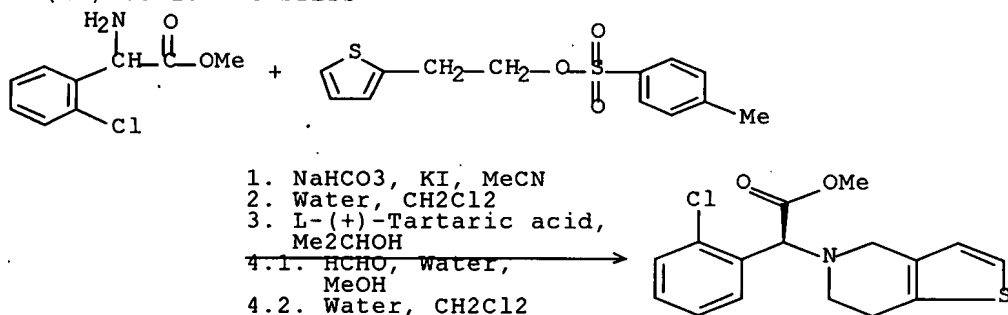
GI



AB The invention provides an improved process for the preparation of the (S)-isomer of Me α -(4,5,6,7-tetrahydro-5-thieno[3,2-c]pyridyl)- α -(2-chlorophenyl)acetate (I), or a salt thereof. I is the well-known antithrombotic and platelet aggregation inhibitor clopidogrel. The process comprises 4 steps: (a) resolving racemic Me α -[[2-(thien-2-yl)ethyl]amino]- α -(2-chlorophenyl)acetate (II) or a salt to obtain (S)-II or a salt and (R)-II or a salt; (b) racemizing (R)-II or a salt to obtain racemic II and optionally converting it into a salt; (c) optionally repeating steps a and b; and (d) converting (S)-II obtained in step a to I. The invention provides a simple process whereby unwanted isomers and derivs. that may be generated during resolution of II can be converted back to racemic II and recycled to produce the desired dextrorotatory isomer (S)-II, which is then converted to clopidogrel. Surprisingly, control of key parameters like concentration, agitation, and cooling during resolution provides the desired (S)-(+)-II tartrate salt in a single operation, directly from the reaction mixture, avoiding repetitive crystns. The other isomer (R)-II and derivs. of II remain

in the mother liquor in the form of an enantiomerically enriched mixture, which can be converted to racemic II, which can then be further recycled. In synthetic examples, DL-2-chlorophenylglycine Me ester was N-alkylated with 2-(2-thiophene)ethanol tosylate using NaHCO₃ and KI in MeCN at 80° to give racemic II.HCl. This salt was neutralized with Na₂CO₃ between aqueous and CH₂Cl₂ layers, and the concentrated free base was resolved using (L)-(+)-tartaric acid (III) in iso-PrOH to give crystalline (S)-II.III with typical [α]_D > +88°. The residue from the mother liquors containing (R)-II was racemized by sequential treatment with NaOMe in MeOH at 65-70°, followed by HCl in MeOH at 5-10°, a catalytic amount of DMF, and then SOCl₂ at 5-15°, followed by warming to 30-35° and continued stirring. Workup and acidification gave crystalline racemic II.HCl. Meanwhile, (S)-II was freed from the above tartrate salt as the HCl salt, which was cyclocondensed with aqueous formaldehyde at 55° to give I free base. Treatment of I with H₂SO₄ in acetone gave clopidogrel bisulfate, [α]_D=+56° (20°, c=1, MeOH).

RX(10) OF 10 - 4 STEPS



NOTE: 1) workup, 3) stereoselective, workup, resolution
 CON: STEP(1.1) 24 hours, 80 deg C; 80 deg C; 24 hours, 80 deg C
 STEP(2.1) 30 - 35 deg C; 15 minutes, 30 - 35 deg C
 STEP(3.1) 30 - 35 deg C; 35 deg C -> 55 deg C; 2 hours, 65 - 70 deg C
 STEP(4.1) 55 deg C; 3 - 4 hours, 55 deg C; 55 deg C -> 30 deg C

L61 ANSWER 2 OF 31 CASREACT COPYRIGHT 2007 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 138:106680 CASREACT Full-text
 TITLE: Process for the preparation of tetrahydrothieno[3,2-c]pyridine derivatives, particularly ticlopidine and clopidogrel, via novel intermediates
 INVENTOR(S): Horne, Stephen E.; Weeratunga, Gamini; Comanita, Bogdan M.; Nagireddy, Jaipal Reddy; McConachie, Laura Kaye
 PATENT ASSIGNEE(S): Brantford Chemicals Inc., Can.
 SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004502	A1	20030116	WO 2002-CA1017	20020705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

CA 2352520	A1	20030106	CA 2001-2352520	20010706
AU 2002317106	A1	20030121	AU 2002-317106	20020705
EP 1404681	A1	20040407	EP 2002-745008	20020705

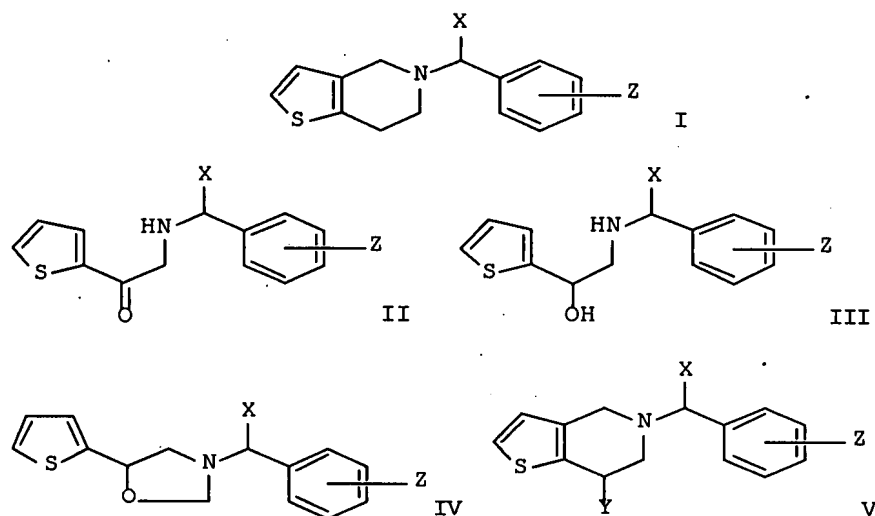
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:

CA 2001-2352520	20010706
WO 2002-CA1017	20020705

OTHER SOURCE(S): MARPAT 138:106680

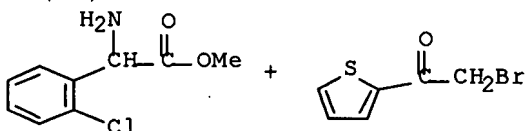
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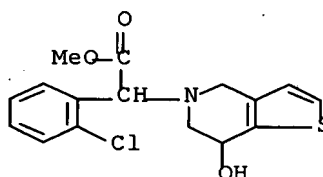
AB A process for the preparation of tetrahydrothieno[3,2-c]pyridine derivs. I and their pharmaceutically acceptable salts is disclosed [wherein: X = H, CO₂H, alkoxy-carbonyl, aryloxy-carbonyl, nitrile, or CONR₁R₂; R₁, R₂ = H, alkyl, or part of a heterocycle; Z = H, halo, alkyl, aryl, aryloxy, or alkoxy]. Comps. I include the com. important drugs ticlopidine and clopidogrel, useful as antithrombotics and platelet aggregation inhibitors. The method comprising the steps of: (a) reduction of amino ketones II with suitable reducing agents to obtain amino alcs. III, (b) cyclization of III with formaldehyde (or any chemical equivalent) to obtain oxazolidines IV, (c) rearrangement of IV to produce the (hydr)oxy-substituted tetrahydrothienopyridines V [Y = OH, alkanoyloxy, aryloxy, carbamate or carbonate derivs.], and (d) reduction of V to give I. Synthetic examples are given for the preparation of racemic and (S)-isomeric clopidogrel. For instance, reaction of (S)-Me o-chlorophenylglycinate with 2-(bromoacetyl)thiophene in DMF at room temperature gave (S)-II (X = CO₂Me, Z = o-Cl) with 95:5 enantiomeric ratio. Reduction of this ketone with NaBH₄ in MeOH gave (S,RS)-III as a mixt of diastereomers. This alc. reacted with 37% formalin in EtOH at 40° to give, after evaporation and azeotropic distillation with PhMe, (S,RS)-IV. Rearrangement of the latter

using HCl in dry DMF at 0-35° gave (S,RS)-V, which was reduced by SnCl₂·2H₂O and concentrated HCl in AcOH to give (S)-I (X = CO₂Me, Z = o-Cl), i.e. clopidogrel, with a 98:2 enantiomer ratio. Racemic clopidogrel was prepared likewise. The method uses inexpensive reagents and gives good yields. The novel intermediates in the clopidogrel syntheses and their individual enantiomers are claimed per se.

RX(20) OF 30 - 4 STEPS



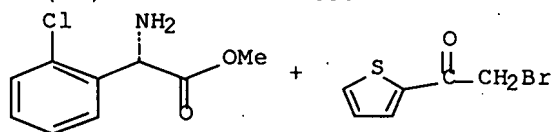
1. K₂CO₃, PhMe, DMF
2. NaBH₄, MeOH
- 3.1. HCHO, EtOH,
Water
- 3.2. PhMe
4. HCl, DMF



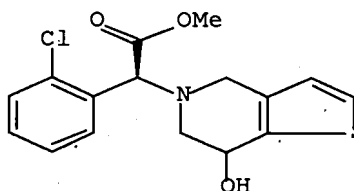
NOTE: 1) monitored to disappearance of starting ester, 2) mixed diastereomers, 3) evapn. in vacuo; azeotropic distn., mixed diastereomers, 4) monitored to disappearance of starting material

CON: STEP(1) 60 deg C
 STEP(2.1) overnight, room temperature
 STEP(3.1) overnight, 40 deg C
 STEP(3.2) reflux
 STEP(4.1) 0 - 5 deg C; 0 deg C -> room temperature;

RX(26) OF 30 - 4 STEPS



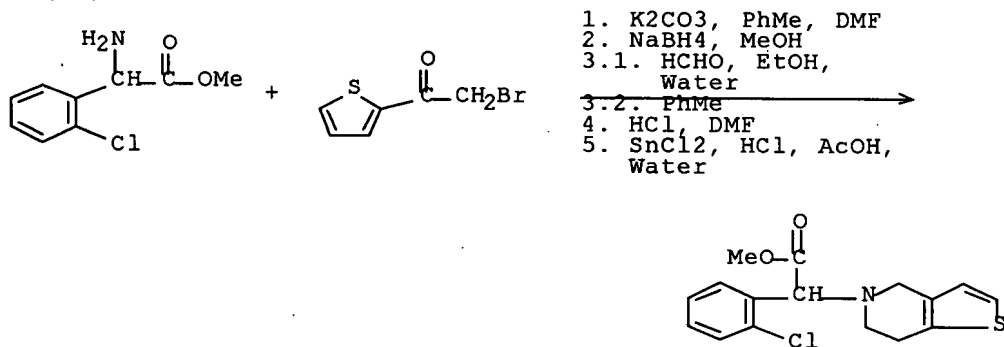
1. K₂CO₃, PhMe, DMF
2. NaBH₄, MeOH
- 3.1. HCHO, EtOH,
Water
- 3.2. PhMe
4. HCl, DMF



NOTE: 1) monitored to disappearance of starting ester, 95:5 enantiomer ratio, 2) mixed diastereomers, 3) evapn. in vacuo; azeotropic distn., mixed diastereomers, 4) monitored to disappearance of starting material, mixed diastereomers

CON: STEP(1) room temperature
 STEP(2.1) 10 deg C; 10 deg C -> room temperature; 2 hours, room temperature
 STEP(3.1) 4 hours, 40 deg C
 STEP(3.2) reflux
 STEP(4.1) 0 - 5 deg C; 0 deg C -> room temperature; overnight, 35 deg C

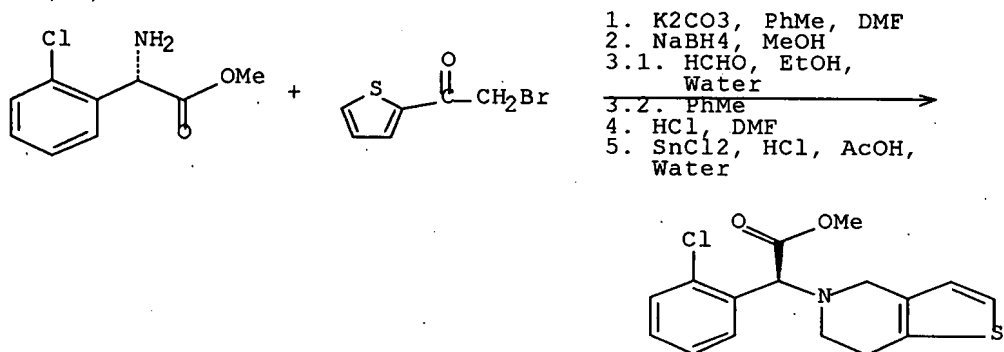
RX(29) OF 30 - 5 STEPS



NOTE: 1) monitored to disappearance of starting ester, 2) mixed diastereomers, 3) evapn. in vacuo; azeotropic distn. mixed diastereomers, 4) monitored to disappearance of starting material

CON: STEP(1) 60 deg C
 STEP(2.1) overnight, room temperature
 STEP(3.1) overnight, 40 deg C
 STEP(3.2) reflux
 STEP(4.1) 0 - 5 deg C; 0 deg C -> room temperature; room temperature
 STEP(5) overnight

RX(30) OF 30 - 5 STEPS



NOTE: 1) monitored to disappearance of starting ester, 95:5 enantiomer ratio, 2) mixed diastereomers, 3) evapn. in vacuo; azeotropic distn., mixed diastereomers, 4) monitored to disappearance of starting material, mixed diastereomers, 5) monitored to completion, 98:2 enantiomer ratio

CON: STEP(1) room temperature
 STEP(2.1) 10 deg C; 10 deg C -> room temperature; 2 hours,
 room temperature
 STEP(3.1) 4 hours, 40 deg C
 STEP(3.2) reflux
 STEP(4.1) 0 - 5 deg C; 0 deg C -> room temperature; overnight,
 35 deg C

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 31 CASREACT COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 138:24949 CASREACT Full-text

TITLE: Process for the preparation of tetrahydrothieno[3,2-c]pyridine derivatives

INVENTOR(S): Horne, Stephen E.; Weeratunga, Gamini; Comanita, Bogdan M.; Nagireddy, Jaipal Reddy; McConachie, Laura Kaye

PATENT ASSIGNEE(S): Brantford Chemicals Inc., Can.

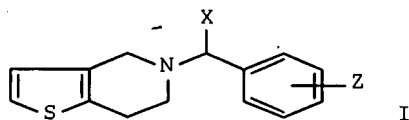
SOURCE: U.S., 10 pp.
 CODEN: USXXAM

DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

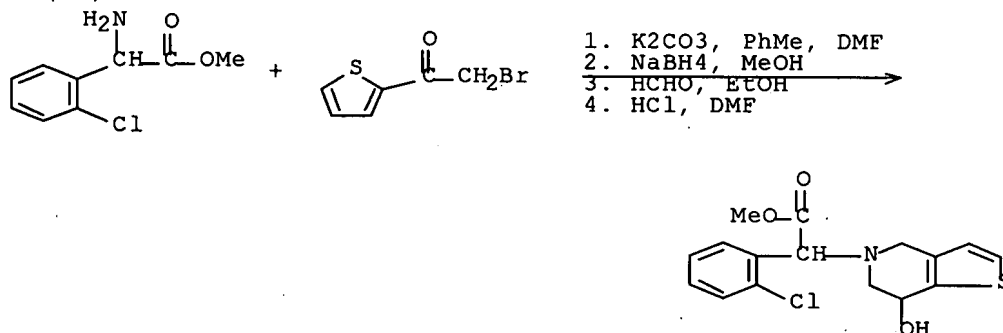
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6495691	B1	20021217	US 2001-902165	20010711
PRIORITY APPLN. INFO.:			US 2001-902165	20010711
OTHER SOURCE(S):	MARPAT 138:24949			
GI				



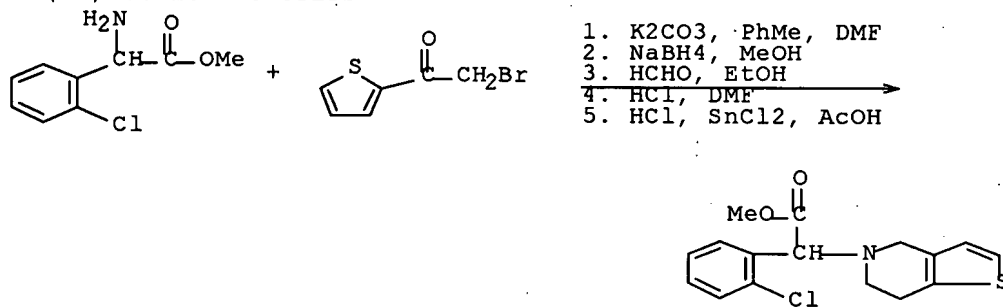
AB Tetrahydrothieno[3,2-c]pyridine derivs. I [X = carboxyl, alkoxycarbonyl, aryloxy carbonyl, or carbamoyl; Z = H, halo, alkyl, aryl, aryloxy, or alkoxy] or their pharmaceutically-acceptable salts were prepared from N-[2-(2-thienyl)-2-oxoethyl]-2-phenylglycinate derivs. Thus, treatment of 2-(bromoacetyl)thiophene with Me (o-chlorophenyl)glycinate in toluene-DMF in the presence of K₂CO₃ afforded Me N-[2-(2-thienyl)-2-oxoethyl]-2-(o-

chlorophenyl)glycinate. The latter underwent borohydride reduction of the oxo group, cyclocondensation with formalin, treatment of the 1,3-oxazoline derivative with HCl in dry DMF, and dehydroxylation with HCl and SnCl₂ in acetic acid to afford I (X = CO₂Me, Z = 2-Cl).

RX(12) OF 15 - 4 STEPS



RX(15) OF 15 - 5 STEPS



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

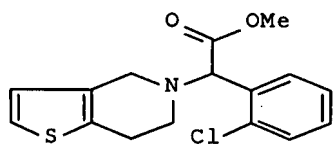
L61 ANSWER 4 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2007:327700 ZCAPLUS Full-text
 DOCUMENT NUMBER: 146:337872

TITLE: Process for preparation of methyl (+)-(S)- α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetate (clopidogrel) via cyclocondensation of methyl (+)- α -(2-thienylethylamino)-N-(2-chlorophenyl)acetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid.
 INVENTOR(S): Srivastava, Anita Ranjan; Pawar, Prashant Pandurang;

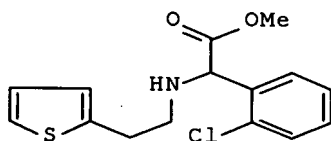
Poojari, Krishna Anand; Patil, Pravin Chaitram; Dalvi, Rajiv Ramchandra
 PATENT ASSIGNEE(S): RPG Life Sciences Limited, India
 SOURCE: PCT Int. Appl., 24pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007032023	A2	20070322	WO 2006-IN250	20060707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: IN 2005-MU836 A 20050709
 OTHER SOURCE(S): CASREACT 146:337872
 GI



I



II

- AB A process for preparation of clopidogrel (I) comprises reaction of Me (S)- α -(2-thienylethylamino)-N-(2-chlorophenyl)acetate (II) salt with H₂CO in H₂O in the presence of catalytic hydrochloric acid under heating followed by separation of the aqueous layer from the sticky mass, extraction of the aqueous layer with petroleum ether or hexane at pH 2-3, and concentration of the organic layer. Thus, II.HCl, H₂CO, and cat. HCl were heated together in H₂O at 78-80° for 2 h; the aqueous layer was separated and extracted twice with petroleum ether to give after concentration 83.57% I of 99.90% purity.
- CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 45
- IT **113665-84-2P**, Clopidogrel
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation clopidogrel via cyclocondensation of Me thienylethylaminochlorophenylacetate salt with paraformaldehyde in the presence of catalytic hydrochloric acid)
- IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)

(preparation clopidogrel via cyclocondensation of Me
thienylethylaminochlorophenylacetate salt with paraformaldehyde in the
presence of catalytic hydrochloric acid)

IT 7664-41-7, Ammonia, reactions **7664-93-9**, Sulfuric acid,
reactions

RL: **RGT (Reagent); RACT (Reactant or reagent)**

(preparation clopidogrel via cyclocondensation of Me
thienylethylaminochlorophenylacetate salt with paraformaldehyde in the
presence of catalytic hydrochloric acid)

IT **113665-84-2P**, Clopidogrel

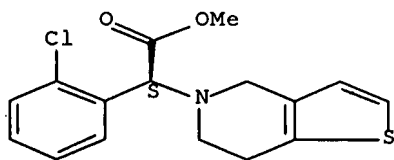
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation clopidogrel via cyclocondensation of Me
thienylethylaminochlorophenylacetate salt with paraformaldehyde in the
presence of catalytic hydrochloric acid)

RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)

(preparation clopidogrel via cyclocondensation of Me
thienylethylaminochlorophenylacetate salt with paraformaldehyde in the
presence of catalytic hydrochloric acid)

RN 120202-66-6 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

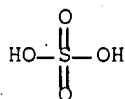
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



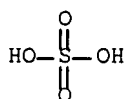
IT 7664-93-9, Sulfuric acid, reactions

RL: **RGT (Reagent); RACT (Reactant or reagent)**

(preparation clopidogrel via cyclocondensation of Me
thienylethylaminochlorophenylacetate salt with paraformaldehyde in the
presence of catalytic hydrochloric acid)

RN 7664-93-9 ZCAPLUS

CN Sulfuric acid (CA INDEX NAME)



L61 ANSWER 5 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:281991 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:337870

TITLE: Process for preparation of clopidogrel and analogues

INVENTOR(S): Wang, Lixin; Tang, Yi; Cheng, Yi; Tian, Fang

PATENT ASSIGNEE(S): Zhejiang Huahai Pharmaceutical Co., Ltd., Peop. Rep.
China; Chengdu Organic Chemicals Co., Ltd., Chinese
Academy of Sciences

SOURCE: PCT Int. Appl., 73pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

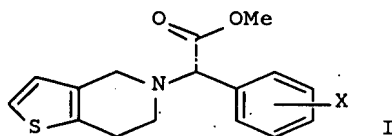
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007028337	A1	20070315	WO 2006-CN2316	20060907
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,			

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

CN 1927863	A	20070314	CN 2005-10060719	20050908
CN 1927864	A	20070314	CN 2005-10060720	20050908
CN 1927865	A	20070314	CN 2005-10060721	20050908
CN 1927866	A	20070314	CN 2005-10060722	20050908
CN 1951940	A	20070425	CN 2005-10061230	20051021
CN 1951941	A	20070425	CN 2005-10061231	20051021
PRIORITY APPLN. INFO.:			CN 2005-10060719	A 20050908
			CN 2005-10060720	A 20050908
			CN 2005-10060721	A 20050908
			CN 2005-10060722	A 20050908
			CN 2005-10061230	A 20051021
			CN 2005-10061231	A 20051021

OTHER SOURCE(S): MARPAT 146:337870
GI



- AB This invention provides a process for preparing optically active clopidogrel and its analogs I [wherein X = H, F, Cl, Br, or I] comprising kinetic resolution of racemates. For example, racemic 2-chlorophenyl-(6,7-dihydro-4H-thieno[3,2-c]pyrid-5-yl)acetonitrile (preparation given) was methylated with di-Me sulfate in the presence of potassium hydroxide and triethylbenzylammonium chloride to give racemic clopidogrel. The obtained racemic clopidogrel was reacted with D-camphorsulfonic acid to give (S)-clopidogrel salt with high purity. The (R)-clopidogrel can be recycled by racemization in aqueous solution in the presence of base and phase transfer catalyst.
- CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
- IT 113665-84-2P 120202-65-5P 120202-66-6P
120202-67-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(preparation of clopidogrel and analogs)
- IT 7647-01-0, Hydrochloric acid, reactions 7664-93-9, Sulfuric acid, reactions 10035-10-6, Hydrobromic acid, reactions
RL: **RCT (Reactant)**; **RGT (Reagent)**; **RACT (Reactant or reagent)**
(preparation of clopidogrel and analogs)
- IT 113665-84-2P 120202-65-5P 120202-66-6P
120202-67-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)
(preparation of clopidogrel and analogs)
- RN 113665-84-2 ZCAPLUS
- CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-

dihydro-, methyl ester, (α S)- (CA INDEX NAME)

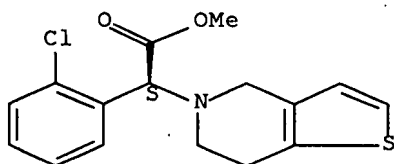
Absolute stereochemistry. Rotation (+).



RN 120202-65-5 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, hydrochloride (1:1), (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

RN 120202-66-6 ZCAPLUS

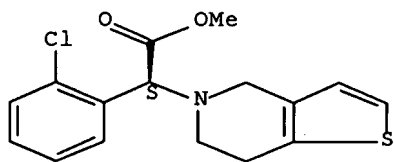
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

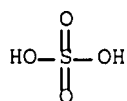
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

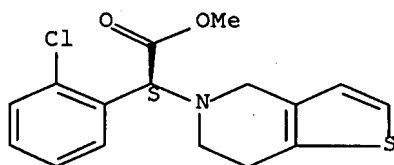
CMF H2 O4 S



RN 120202-67-7 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, hydrobromide (1:1), (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HBr

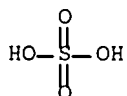
IT 7664-93-9, Sulfuric acid, reactions

RL: *RCT (Reactant)*; *RGT (Reagent)*; *RACT (Reactant or reagent)*

(preparation of clopidogrel and analogs)

RN 7664-93-9 ZCAPLUS

CN Sulfuric acid (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 6 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:126526 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:280791

TITLE: Method for preparing I type clopidogrel bisulfate

INVENTOR(S): Mao, Haifang; Pan, Xianhua

PATENT ASSIGNEE(S): Shanghai Institute of Technology, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1903859	A	20070131	CN 2006-10029489	20060728
PRIORITY APPLN. INFO.:			CN 2006-10029489	20060728

AB The title method includes: (1) mixing clopidogrel salt and organic solvent under dried air or inert gas protection, adding water, reacting with sodium carbonate or potassium carbonate under stirring for 1 h, standing for layering when pH of the upper-layer solution is higher than 7, separating organic phase, extracting water phase with organic solvent, combining organic phase, and recovering solvent to obtain free clopidogrel base, wherein clopidogrel salt is selected from clopidogrel camphor sulfonate, clopidogrel hydrochloride, clopidogrel hydrobromide, or clopidogrel sulfate, and the organic solvent is selected from dichloromethane, dichloroethane, or Et ether, and (2) adding ketone into free clopidogrel base, stirring to dissolve completely, cooling to (-15)-25°, dropping ketone-diluted sulfuric acid or undiluted sulfuric acid at a sulfuric acid/free clopidogrel base molar ratio of 0.6-1.1 while controlling temperature of (-15)-25°, heating to 20-50° after dropping is finished, maintaining the temperature for 0.5-3 h under stirring, filtering, washing, and vacuum-drying at 50-55° to obtain I type clopidogrel bisulfate, wherein the ketone is selected from five-carbon ketone or six-carbon ketone. 20 12-14° chromatogram results of the obtained product and I type clopidogrel bisulfate standard sample containing 0.5% II type clopidogrel bisulfate show that the obtained product contains no II type clopidogrel bisulfate, therefore I type cloridogrel bisulfate. This invention adds seed crystal during crystallization to accelerate crystallization, so that crystallization is finished within 5 h.

CC 63-4 (Pharmaceuticals)

IT **120202-66-6P**, Clopidogrel bisulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(method for preparing I type clopidogrel bisulfate)

IT **7664-93-9**, Sulfuric acid, reactions **120202-65-5**, Clopidogrel hydrochloride **120202-67-7**, Clopidogrel hydrobromide 862163-72-2

RL: **RCT (Reactant)**; **RAC (Reactant or reagent)**

(method for preparing I type clopidogrel bisulfate)

IT **120202-66-6P**, Clopidogrel bisulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(method for preparing I type clopidogrel bisulfate)

RN 120202-66-6 ZCAPLUS

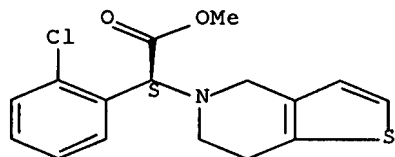
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

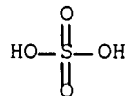
Absolute stereochemistry. Rotation (+).



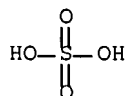
CM 2

CRN 7664-93-9

CMF H2 O4 S

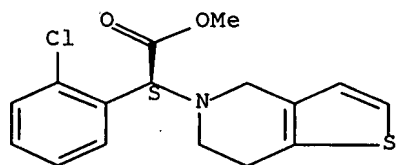


IT 7664-93-9, Sulfuric acid, reactions 120202-65-5,
Clopidogrel hydrochloride 120202-67-7, Clopidogrel hydrobromide
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(method for preparing I type clopidogrel bisulfate)
RN 7664-93-9 ZCAPLUS
CN Sulfuric acid (CA INDEX NAME)



RN 120202-65-5 ZCAPLUS
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, hydrochloride (1:1), (α S)- (CA INDEX NAME)

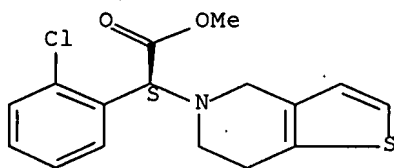
Absolute stereochemistry. Rotation (+).



● HCl

RN 120202-67-7 ZCAPLUS
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, hydrobromide (1:1), (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HBr

L61 ANSWER 7 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1354002 ZCAPLUS Full-text
 DOCUMENT NUMBER: 146:100660
 TITLE: Process for preparation of clopidogrel and intermediates used herein
 INVENTOR(S): Kim, Eun Sook; Kim, Hee Cheol; Kwon, Bo Sung; Yun, Sangmin; Ko, Mi Young; Kim, Cheol Kyung; Suh, Kwee Hyun
 PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
 SOURCE: PCT Int. Appl., 25pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006137628	A1	20061228	WO 2005-KR4017	20051128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: KR 2005-54303 A 20050623
 OTHER SOURCE(S): MARPAT 146:100660

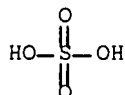
AB This invention provides a process for the preparation of clopidogrel and intermediates used herein, which comprises optically resolving racemic α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid (preparation given) using chiral amines followed by methylation. The process has the advantages of high purity and high yield.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 45

IT 75-75-2, Methanesulfonic acid 104-15-4, 4-Methylbenzenesulfonic acid, uses 7647-01-0, Hydrochloric acid, uses 7664-93-9, Sulfuric acid, uses
 RL: CAT (Catalyst use); USES (Uses)
 (preparation of clopidogrel and intermediates used herein)

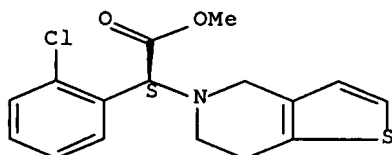
IT 716-61-0P 113665-84-2P, Clopidogrel

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and intermediates used herein)
 IT **120202-66-6P**, Clopidogrel hydrogen sulfate 868560-74-1P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)
 (preparation of clopidogrel and intermediates used herein)
 IT **7664-93-9**, Sulfuric acid, uses
 RL: CAT (Catalyst use); USES (Uses)
 (preparation of clopidogrel and intermediates used herein)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



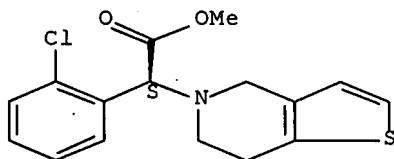
IT **113665-84-2P**, Clopidogrel
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and intermediates used herein)
 RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **120202-66-6P**, Clopidogrel hydrogen sulfate
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)
 (preparation of clopidogrel and intermediates used herein)
 RN 120202-66-6 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)
 CM 1
 CRN 113665-84-2
 CMF C16 H16 Cl N O2 S

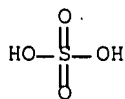
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 8 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1283501 ZCAPLUS Full-text
 DOCUMENT NUMBER: 146:27816
 TITLE: Recovery of resolved clopidogrel bisulfate
 INVENTOR(S): Sajja, Eswaraiah; Anumula, Raghupathi Reddy; Gilla, Goverdhan; Nomula, Muralidhar Reddy
 PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
 SOURCE: PCT Int. Appl., 16pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006130852	A1	20061207	WO 2006-US21548	20060602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			IN 2005-CH679	A 20050602
			US 2005-718786P	P 20050920

AB A process for preparing a racemic clopidogrel acid salt comprises reacting clopidogrel camphor sulfonic acid with an acid. The clopidogrel camphor sulfonic acid can be present in a residue from separating a clopidogrel camphorsulfonic acid optical isomer.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 497-19-8, Sodium carbonate **7664-93-9**, Sulfuric acid, reactions 35963-20-3, (-)-Camphorsulfonic acid
 RL: **RGT (Reagent); RACT (Reactant or reagent)**
 (recovery of resolved clopidogrel bisulfate)

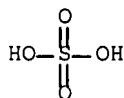
IT **113665-84-2P**, Clopidogrel 862163-72-2P
 RL: RGT (Reagent); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (recovery of resolved clopidogrel bisulfate)

IT **120202-66-6P**, Clopidogrel bisulfate 120202-70-2P
 RL: SPN (Synthetic preparation); **PREP (Preparation)**
 (recovery of resolved clopidogrel bisulfate)

IT **7664-93-9**, Sulfuric acid, reactions
 RL: **RGT (Reagent); RACT (Reactant or reagent)**
 (recovery of resolved clopidogrel bisulfate)

RN 7664-93-9 ZCAPLUS

CN Sulfuric acid (CA INDEX NAME)

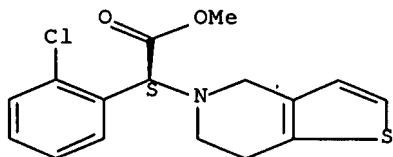


IT **113665-84-2P**, Clopidogrel
 RL: RGT (Reagent); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (recovery of resolved clopidogrel bisulfate)

RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **120202-66-6P**, Clopidogrel bisulfate
 RL: SPN (Synthetic preparation); **PREP (Preparation)**
 (recovery of resolved clopidogrel bisulfate)

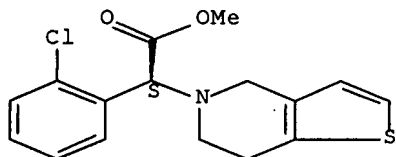
RN 120202-66-6 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

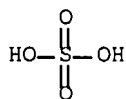
CRN 113665-84-2
CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
CMF H2 O4 S



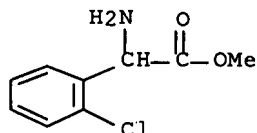
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 9 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:31435 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:108598
TITLE: A process for resolution of methyl
amino(2-chlorophenyl)acetate
INVENTOR(S): Battula, Srinivasa Reddy
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006003671	A1	20060112	WO 2004-IN193	20040702
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD,			

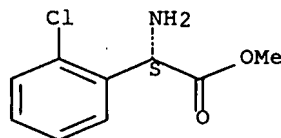
OTHER SOURCE(S): MARPAT 144:108598

- AB Racemic (2-substituted phenyl)glycine or esters were resolved via formation of the salt with L-(+)-tartaric acid (molar ratio 0.9 to 1.4) in acetone, methanol, ethanol, iso-Pr alc. or their mixts. Thus, racemic Me amino(2-chlorophenyl)acetate was resolved by treatment with 1.1 molar equivalent L-(+)-tartaric acid in acetone-methanol and treating an aqueous CH₂Cl₂ solution of the salt with aqueous ammonia to adjust the pH to 6.9-7.1.
- IC ICM C07C227-36
ICS C07C227-40; C07C229-36
- CC 34-2 (Amino Acids, Peptides, and Proteins)
- IT **141109-13-9**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(resolution of (chlorophenyl)glycinate)
- IT **141109-14-0P**
RL: PUR (Purification or recovery); PREP (Preparation)
(resolution of (chlorophenyl)glycinate)
- IT **141109-15-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(resolution of (chlorophenyl)glycinate)
- IT **141109-13-9**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(resolution of (chlorophenyl)glycinate)
- RN 141109-13-9 ZCAPLUS
- CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME)



- IT **141109-14-0P**
RL: PUR (Purification or recovery); PREP (Preparation)
(resolution of (chlorophenyl)glycinate)
- RN 141109-14-0 ZCAPLUS
- CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



- IT **141109-15-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(resolution of (chlorophenyl)glycinate)

RN 141109-15-1 ZCAPLUS

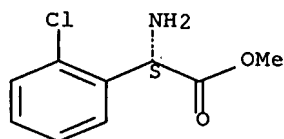
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 141109-14-0

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (+).

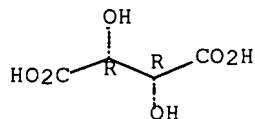


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 10 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:99475 ZCAPLUS Full-text

DOCUMENT NUMBER: 146:401955

TITLE: Synthesis of thiophene derivative as intermediate of
clopidogrel

INVENTOR(S): Oh, Min Keun; Kim, Ki Nam; Choi, Hun

PATENT ASSIGNEE(S): Hanseo Chemical Co., Ltd., S. Korea

SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given

CODEN: KRXXA7

DOCUMENT TYPE: Patent

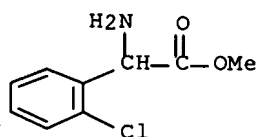
LANGUAGE: Korean

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

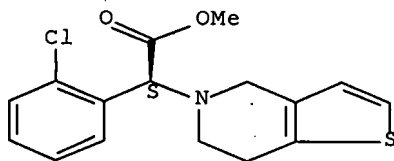
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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KR 2006098009	A	20060918	KR 2005-19068	20050308

- AB A novel thiophene derivative as an intermediate of clopidogrel [i.e., (α S)- α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid Me ester] is claimed. Also claimed is a manufacturing process for clopidogrel using that intermediate compound. Said process provides an improved production yield and purity of clopidogrel, reduces the production costs of clopidogrel with such an inexpensive intermediate. An intermediate (as represented by a certain formula; no data) is claimed. The manufacturing process of clopidogrel comprises the preparation of a chiral compound (as represented by a certain formula; no data) from racemic Me α -amino-(2-chlorophenyl)acetate by using an asym. transformation. Said process comprises acylating said intermediate with 2-thiopheneacetic acid to provide a dextrorotatory Me 2-chloro- α -[(thienyl)acetamido]benzeneacetic acid ester (as represented by a certain formula; no data). Said method also comprises said amido function to provide a suitable intermediate which is cyclized to provide clopidogrel. More narrow definitions are indicated; however, specific chemical structures and/or addnl. information are not provided here.
- CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 27
- IT 1918-77-0, 2-Thiopheneacetic acid **141109-13-9**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation of chloro[(thienyl)methyl]amino]benzeneacetic acid ester for use as intermediate for clopidogrel (platelet aggregation inhibitor))
- IT 110-02-1DP, Thiophene, derivs. **113665-84-2P**, Clopidogrel
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of chloro[(thienyl)methyl]amino]benzeneacetic acid ester for use as intermediate for clopidogrel (platelet aggregation inhibitor))
- IT **141109-13-9**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation of chloro[(thienyl)methyl]amino]benzeneacetic acid ester for use as intermediate for clopidogrel (platelet aggregation inhibitor))
- RN 141109-13-9 ZCAPLUS
- CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME)



- IT **113665-84-2P**, Clopidogrel
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of chloro[(thienyl)methyl]amino]benzeneacetic acid ester for use as intermediate for clopidogrel (platelet aggregation inhibitor))
- RN 113665-84-2 ZCAPLUS
- CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L61 ANSWER 11 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:837726 ZCAPLUS Full-text

DOCUMENT NUMBER: 145:249191

TITLE: Process for preparing clopidogrel hydrogensulfate of polymorphic crystal form I

INVENTOR(S): Ruzic, Milos; Kotar-Jordan, B.; Smrkolj, Matej; Gerksic, Samo; Vrancic, Damir; Benedik, Milena; Gricar, Mira

PATENT ASSIGNEE(S): Krka, Tovarna Zdravil, d.d., Novo Mesto, Slovenia

SOURCE: Eur. Pat. Appl., 7pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1693375	A1	20060823	EP 2005-3654	20050221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
WO 2006087226	A1	20060824	WO 2006-EP1513	20060220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2005-3654 A 20050221

AB A process for the preparation of form I of clopidogrel hydrogensulfate through suspending clopidogrel hydrogensulfate in an alkane (e.g., heptane) is described.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63, 75

IT **120202-66-6P**, Clopidogrel bisulfate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); **PREP (Preparation)**; PROC (Process)

(process for preparing clopidogrel hydrogensulfate of polymorphic crystal form I)

IT **7664-93-9**, Sulfuric acid, reactions **113665-84-2**, Clopidogrel

RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**

(process for preparing clopidogrel hydrogensulfate of polymorphic crystal form I)

IT 120202-66-6P, Clopidogrel bisulfate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); **PREP (Preparation)**; PROC (Process)

(process for preparing clopidogrel hydrogensulfate of polymorphic crystal form I)

RN 120202-66-6 ZCAPLUS

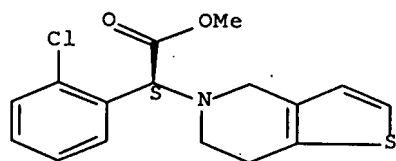
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

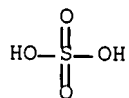
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



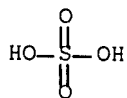
IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel

RL: **RCT (Reactant)**; **RAC (Reactant or reagent)**

(process for preparing clopidogrel hydrogensulfate of polymorphic crystal form I)

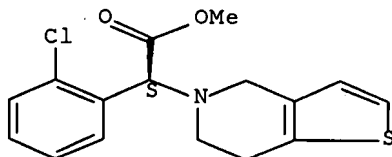
RN 7664-93-9 ZCAPLUS

CN Sulfuric acid (CA INDEX NAME)



RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 12 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:504896 ZCAPLUS Full-text
 DOCUMENT NUMBER: 145:83300
 TITLE: Process for preparation of clopidogrel and its salt
 INVENTOR(S): Mao, Haifang; Pan, Xianhua; Lu, Jiaqing
 PATENT ASSIGNEE(S): Shanghai Institute of Technology, Peop. Rep. China
 SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
 CODEN: CNXXEV
 DOCUMENT TYPE: Patent
 LANGUAGE: Chinese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1775782	A	20060524	CN 2005-10111562	20051215
PRIORITY APPLN. INFO.:			CN 2005-10111562	20051215

AB The title preparation includes esterifying (R)-2-bromo-2-(2-chlorophenyl)acetic acid with methanol in the presence of sulfuric acid or thionyl chloride to generate Me (R)-2-bromo-2-(2-chlorophenyl)acetate; and reacting Me (R)-2-bromo-2-(2-chlorophenyl)acetate with 4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the presence of base to generate the target product. Further neutralization of the product using an acid can result in corresponding salt.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

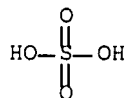
IT **7664-93-9**, Sulfuric acid, reactions
 RL: CAT (Catalyst use); **RCT (Reactant)**; **RACT (Reactant or reagent)**; USES (Uses)
 (preparation of clopidogrel and its salt)

IT **113665-84-2P** 622835-93-2P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and its salt)

IT **120202-65-5P 120202-66-6P** 862163-72-2P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
 (preparation of clopidogrel and its salt)

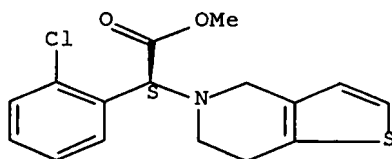
IT **7664-93-9**, Sulfuric acid, reactions
 RL: CAT (Catalyst use); **RCT (Reactant)**; **RACT (Reactant or reagent)**; USES (Uses)

(preparation of clopidogrel and its salt)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



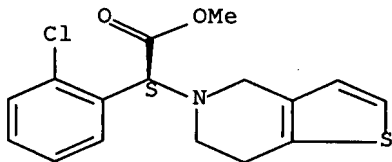
IT **113665-84-2P**
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of clopidogrel and its salt)
 RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **120202-65-5P 120202-66-6P**
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)
 (preparation of clopidogrel and its salt)
 RN 120202-65-5 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, hydrochloride (1:1), (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

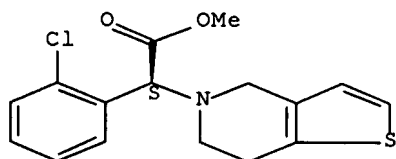
RN 120202-66-6 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

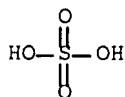
Absolute stereochemistry. Rotation (+).



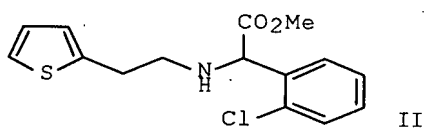
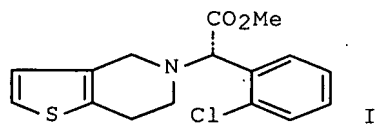
CM 2

CRN 7664-93-9

CMF H2 O4 S



L61 ANSWER 13 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:504294 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:274247
TITLE: Process for preparation of (+)-clopidogrel hydrogen sulfate
AUTHOR(S): Balicki, Roman
CORPORATE SOURCE: Inst. Farm., Warsaw, 01-793, Pol.
SOURCE: Przemysl Chemiczny (2006), 85(5), 342-343
CODEN: PRCHAB; ISSN: 0033-2496
PUBLISHER: Wydawnictwo SIGMA-NOT
DOCUMENT TYPE: Journal
LANGUAGE: Polish
GI



AB The title compound (I·H₂SO₄) was prepared in 3 steps from amino ester II; the desired enantiomer was separated using (-)-camphorsulfonic acid. II was prepared via a convergent route starting from 2-chlorobenzaldehyde and 2-thiopheneethanol.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **141109-13-9P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RCT (Reactant or reagent)**
(intermediate, alkylation by thienylethyl tosylate; preparation of (+)-clopidogrel hydrogen sulfate)

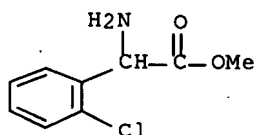
IT **90055-48-4P 120202-68-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RCT (Reactant or reagent)
(preparation of (+)-clopidogrel hydrogen sulfate)

IT **120202-66-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of (+)-clopidogrel hydrogen sulfate)

IT **141109-13-9P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RCT (Reactant or reagent)**
(intermediate, alkylation by thienylethyl tosylate; preparation of (+)-clopidogrel hydrogen sulfate)

RN 141109-13-9 ZCAPLUS

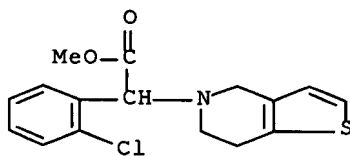
CN Benzeneacetic acid, α-amino-2-chloro-, methyl ester (CA INDEX NAME)



IT **90055-48-4P 120202-68-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RCT (Reactant or reagent)
(preparation of (+)-clopidogrel hydrogen sulfate)

RN 90055-48-4 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester (CA INDEX NAME)



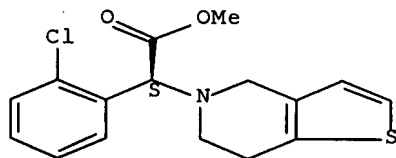
RN 120202-68-8 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, (αS)-, methyl ester(1R,4S)-compd. with 7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonic acid (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2
CMF C16 H16 Cl N O2 S

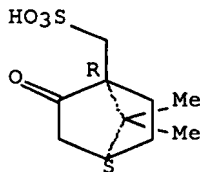
Absolute stereochemistry. Rotation (+).



CM 2

CRN 35963-20-3
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (-).



IT 120202-66-6P

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of (+)-clopidogrel hydrogen sulfate)

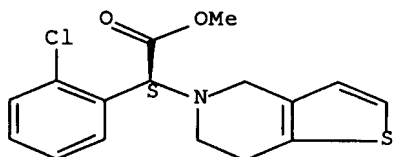
RN 120202-66-6 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

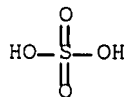
CRN 113665-84-2
CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
CMF H2 O4 S



L61 ANSWER 14 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1154559 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:427350
TITLE: Preparation of clopidogrel hydrogen sulfate
polymorphic form I
INVENTOR(S): Mao, Haifang; Qian, Hongguang; Chen, Chen
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005100364	A1	20051027	WO 2005-EP4160	20050419
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
SI 21749	A	20051031	SI 2004-122	20040421
EP 1740593	A1	20070110	EP 2005-734224	20050419
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU			
NO 2006005321	A	20070109	NO 2006-5321	20061120
PRIORITY APPLN. INFO.:			CN 2004-2004	A 20040419
			SI 2004-122	A 20040421
			CN 2004-10009028	A 20040419
			WO 2005-EP4160	W 20050419

AB Processes for the preparation of clopidogrel (I) hydrogen sulfate of polymorphic form I are described which include use of specific solvents and process measures to avoid formation of undesired byproducts. I-HCl or a crystalline mixture of I H sulfate or I camphor sulfate is neutralized with a

base such as K₂CO₃ to give I base and then an organic solvent solution treatment with concn H₂SO₄.

IC ICM C07D495-04

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 28

IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT 584-08-7, Potassium carbonate **7664-93-9**, Sulfuric acid, reactions **120202-65-5**, Clopidogrel hydrochloride 120202-68-8

RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**

(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT **113665-84-2P**, Clopidogrel

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of clopidogrel hydrogen sulfate polymorphic form I)

IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(preparation of clopidogrel hydrogen sulfate polymorphic form I)

RN 120202-66-6 ZCAPLUS

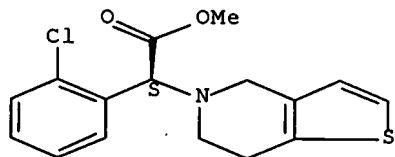
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

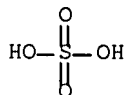
Absolute stereochemistry. Rotation (+).



CM 2

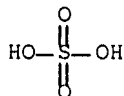
CRN 7664-93-9

CMF H2 O4 S



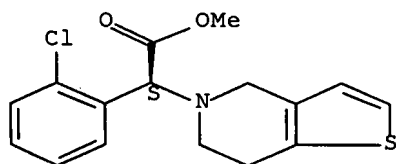
IT **7664-93-9**, Sulfuric acid, reactions **120202-65-5**, Clopidogrel hydrochloride
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**

(preparation of clopidogrel hydrogen sulfate polymorphic form I)
RN 7664-93-9 ZCAPLUS
CN Sulfuric acid (CA INDEX NAME)



RN 120202-65-5 ZCAPLUS
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, hydrochloride (1:1), (α S)- (CA INDEX NAME)

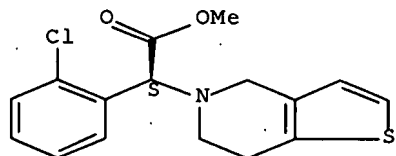
Absolute stereochemistry. Rotation (+).



● HCl

IT **113665-84-2P**, Clopidogrel
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of clopidogrel hydrogen sulfate polymorphic form I)
RN 113665-84-2 ZCAPLUS
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

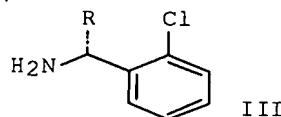
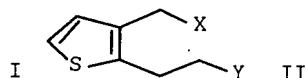
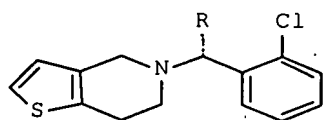


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 15 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1026954 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:326345
TITLE: preparation of chlorobenzylthienopyridines from chlorobenzylamines and hydroxymethylthiopheneethanol

derivatives
 INVENTOR(S): Yun, Sangmin; Kim, Eun Sook; Kim, Hee Seock; Ha, Tae Hee; Suh, Kwee-Hyun; Lee, Gwan Sun
 PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087779	A1	20050922	WO 2005-KR586	20050303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2005091330	A	20050915	KR 2004-16714	20040312
AU 2005222016	A1	20050922	AU 2005-222016	20050303
CA 2559571	A1	20050922	CA 2005-2559571	20050303
EP 1723149	A1	20061122	EP 2005-721898	20050303
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1930172	A	20070314	CN 2005-80008059	20050303
PRIORITY APPLN. INFO.:			KR 2004-16714	A 20040312
			WO 2005-KR586	W 20050303
OTHER SOURCE(S):		MARPAT 143:326345		
GI				



AB Title compds. (I; R = H, MeO₂C), were prepared by reaction of thiophene derivs. (II; X, Y = Cl, Br, mesyloxy, tosyloxy) with chlorobenzylamines (III; R as above). Thus, 2-(2-bromoethyl)-3-bromomethylthiophene (preparation given), 2-chlorobenzylamine, and diisopropylamine were refluxed together for 5 h in MeCN to give 78% Ticlopidine.
 IC ICM C07D495-04
 CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 IT 55142-85-3P, Ticlopidine **113665-84-2P**, Clopidogrel
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
 (Preparation)
 (preparation of chlorobenzylthienopyridines from chlorobenzylamines and

hydroxymethylthiopheneethanol derivs.)

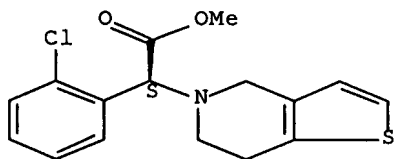
IT 89-97-4, 2-Chlorobenzylamine 110-88-3, 1,3,5-Trioxane, reactions
 646-06-0, 1,3-Dioxolane 1830-54-2, Dimethyl acetonedicarboxylate
 5402-55-1, 2-(2-Thienyl)ethanol 30525-89-4, Paraformaldehyde
 40018-26-6, 2,5-Dihydroxy-1,4-dithiane **213018-92-9**
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (preparation of chlorobenzylthienopyridines from chlorobenzylamines and
 hydroxymethylthiopheneethanol derivs.)

IT **113665-84-2P**, Clopidogrel
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP**
(Preparation)
 (preparation of chlorobenzylthienopyridines from chlorobenzylamines and
 hydroxymethylthiopheneethanol derivs.)

RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
 dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

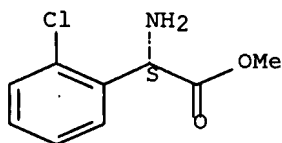


IT **213018-92-9**
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (preparation of chlorobenzylthienopyridines from chlorobenzylamines and
 hydroxymethylthiopheneethanol derivs.)

RN 213018-92-9 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride,
 (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



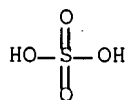
● HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 16 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:120929 ZCAPLUS Full-text
 DOCUMENT NUMBER: 142:204623
 TITLE: A novel process for the manufacture of
 (+)-(s)-clopidogrel bisulfate form-I

INVENTOR(S): Jaweed Mukarram, Siddiqui Mohammed; Merwade, Aravind
 Yekanathsa; Khan, Anjum Reyaz
 PATENT ASSIGNEE(S): Wockhardt Limited, India
 SOURCE: PCT Int. Appl., 9 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

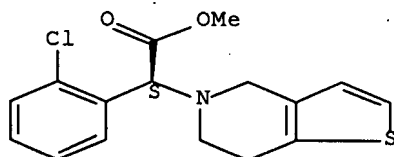
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012300	A1	20050210	WO 2003-IB3104	20030804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2534893	A1	20050210	CA 2003-2534893	20030804
AU 2003253120	A1	20050215	AU 2003-253120	20030804
EP 1651646	A1	20060503	EP 2003-817742	20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
BR 2003018449	A	20060801	BR 2003-18449	20030804
IN 2006MN00088	A	20060929	IN 2006-MN88	20060124
US 2006183907	A1	20060817	US 2006-564364	20060223
PRIORITY APPLN. INFO.:			WO 2003-IB3104	W 20030804
AB	The present invention relates to a novel process for the manufacture of blood-platelet aggregation inhibiting agent. In particular, the present invention is directed to a process for the manufacture of methyl-(+)-(S)- α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-S-(4H)acetate bisulfate Form-I. A solution of 4.50 gm (+)-(S)-clopidogrel in 50 mL Et acetate was seeded with (+)-(S)-clopidogrel bisulfate Form-I (2.5 % of the weight of base). During stirring 1.50 gm concentrate sulfuric acid was added at room temperature and the reaction slurry was heated at reflux for 1 h. Then it was stirred at room temperature for 1 h, the product was then filtered under suction and washed with Et acetate followed by drying under vacuum at 60° to 70° for 6-8 h. After complete drying, 4.0 gm (+)-(S)-clopidogrel bisulfate Form-I was obtained having 99.96 % purity.			
IC	ICM C07D471-04			
CC	63-5 (Pharmaceuticals)			
IT	7664-93-9, Sulfuric acid, reactions 35963-20-3 113665-84-2, (+)-(S)-Clopidogrel RL: RCT (Reactant); RACT (Reactant or reagent) (novel process for manufacture of clopidogrel bisulfate form-I)			
IT	120202-66-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (novel process for manufacture of clopidogrel bisulfate form-I)			
IT	7664-93-9, Sulfuric acid, reactions 113665-84-2, (+)-(S)-Clopidogrel RL: RCT (Reactant); RACT (Reactant or reagent) (novel process for manufacture of clopidogrel bisulfate form-I)			
RN	7664-93-9 ZCAPLUS			
CN	Sulfuric acid (CA INDEX NAME)			



RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 120202-66-6P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**
(Preparation); RACT (Reactant or reagent)

(novel process for manufacture of clopidogrel bisulfate form-I)

RN 120202-66-6 ZCAPLUS

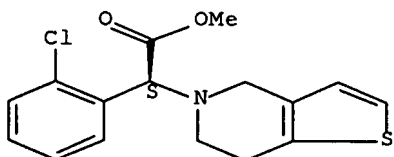
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

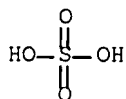
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 17 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:29339 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:141212

TITLE: Process for the preparation of crystalline polymorph of a platelet aggregation inhibitor drug

INVENTOR(S): Kotay Nagy, Peter; Simig, Gyula; Barkoczy, Jozsef; Gregor, Tamas; Farkas, Bela; Vereckeyne Donath, Gyoergyi; Nagy, Kalman; Koertvelyessy, Gyulane; Szent-Kirallyi, Zsuzsanna

PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

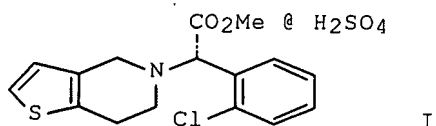
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003139	A1	20050113	WO 2004-HU70	20040630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200401272	A2	20050228	HU 2004-1272	20040623
HU 200401272	A3	20050928		
CA 2530449	A1	20050113	CA 2004-2530449	20040630
EP 1644381	A1	20060412	EP 2004-743729	20040630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812993	A	20060802	CN 2004-80018122	20040630
BG 109429	A	20061031	BG 2006-109429	20060202
PRIORITY APPLN. INFO.:			HU 2003-2028	A 20030702
			HU 2004-1272	A 20040623
			WO 2004-HU70	W 20040630

GI



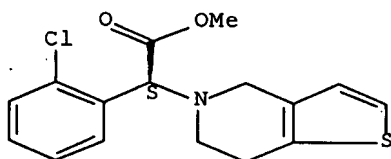
- AB The present invention relates to a new method of preparation of the polymorph form 1 of Me (S)-(+)-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c]pyridine-5-yl)acetate hydrogen sulfate of the formula I. Thus, a solution containing 2.2 g of clopidogrel base in 130 mL acetone is stirred and cooled to 10-15°C, followed by addition of 10.2 g 96% weight/weight% sulfuric acid. The obtained mixture is added to a suspension of 10 g. clopidogrel hydrogensulfate polymorph 1 in 1000 mL diisopropyl ether dropwise at 0°C in 15-20 min with stirring to yield 48 g (90.5%) clopidogrel hydrogensulfate polymorph 1 after filtration, washing, and drying.
- IC ICM C07D495-04
- CC 63-5 (Pharmaceuticals)
- IT **120202-66-6P**, Clopidogrel hydrogensulfate
 RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); **PREP (Preparation)**
 (crystalline polymorph 1; process for preparation of platelet aggregation inhibitor drug crystalline polymorph)
- IT **7664-93-9**, Sulfuric acid, reactions **113665-84-2**, Clopidogrel
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (process for preparation of platelet aggregation inhibitor drug crystalline polymorph)
- IT **120202-66-6P**, Clopidogrel hydrogensulfate
 RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); **PREP (Preparation)**
 (crystalline polymorph 1; process for preparation of platelet aggregation inhibitor drug crystalline polymorph)
- RN 120202-66-6 ZCAPLUS
- CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

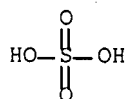
CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).

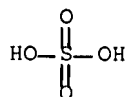


CM 2

CRN 7664-93-9

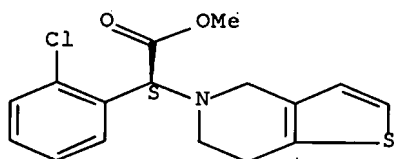


IT 7664-93-9, Sulfuric acid, reactions 113665-84-2,
 Clopidogrel
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (process for preparation of platelet aggregation inhibitor drug crystalline
 polymorph)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
 dihydro-, methyl ester, (α S)- (CA INDEX NAME)

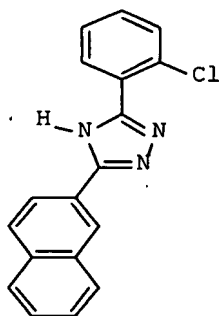
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 18 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:1141816 ZCAPLUS Full-text
 DOCUMENT NUMBER: 142:240378
 TITLE: Polymer-Supported 1,3-Oxazolium-5-olates: Synthesis of
 1,2,4-Triazoles
 AUTHOR(S): Samanta, Swapan K.; Yli-Kauhaluoma, Jari
 CORPORATE SOURCE: Viikki Drug Discovery Technology Center, Faculty of
 Pharmacy, University of Helsinki, Helsinki, FI-00014,
 Finland
 SOURCE: Journal of Combinatorial Chemistry (2005), 7(1),
 142-146
 CODEN: JCCHFF; ISSN: 1520-4766
 PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 142:240378
 GI



AB A traceless synthesis of 3,5-disubstituted 1,2,4-triazoles, e.g., I, has been developed on polymeric supports. The synthetic process utilizes immobilized mesoionic 1,3-oxazolium-5-olates (munchnones) as key intermediates in the 1,3-dipolar cycloaddn. reaction. The initial step in the synthesis involved reductive alkylation of phenylglycine Me esters with Ameba resin. The resulting immobilized amino acid esters were subsequently acylated with a variety of carboxylic acid chlorides and subjected to hydrolysis to yield the polymer-bound carboxylic acids. Finally, the cycloaddn. between di-Et diazocarboxylate or 4-phenyl-4H-1,2,4-triazoline-3,5-dione and the polymer-bound munchnones generated from the corresponding carboxylic acids afforded the polymer-bound 3,5-disubstituted 1,2,4-triazoles. Cleavage from the polymeric support using trifluoroacetic acid gave the desired 3,5-disubstituted 1,2,4-triazoles with excellent yield and high purity.

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 98-88-4, Benzoyl chloride 100-07-2, 4-Methoxybenzoyl chloride
 122-01-0, 4-Chlorobenzoyl chloride 122-04-3, 4-Nitrobenzoyl chloride
 403-43-0, 4-Fluorobenzoyl chloride 874-60-2, 4-Methylbenzoyl chloride
 2243-83-6, 2-Naphthalenecarbonyl chloride 10400-19-8,
 3-Pyridinylcarbonyl chloride 16331-45-6, 4-Ethylbenzoyl chloride
 24461-61-8 49763-65-7, 4-Pentylbenzoyl chloride 52710-27-7,
 4-Propylbenzoyl chloride **141109-16-2**

RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)

(combinatorial preparation of diaryltriazoles via reductive amination of Ameba resin with phenylglycine Me esters followed by amidation with aroyl chlorides, hydrolysis, cyclization, dipolar cycloaddn., and resin cleavage)

IT **141109-16-2**

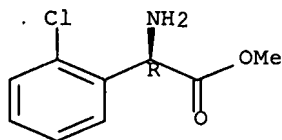
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)

(combinatorial preparation of diaryltriazoles via reductive amination of Ameba resin with phenylglycine Me esters followed by amidation with aroyl chlorides, hydrolysis, cyclization, dipolar cycloaddn., and resin cleavage)

RN 141109-16-2 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 19 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:780708 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:282821

TITLE: Process for the preparation of amorphous clopidogrel hydrogensulfate

INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari

PATENT ASSIGNEE(S): Hetero Drugs Limited, India

SOURCE: PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

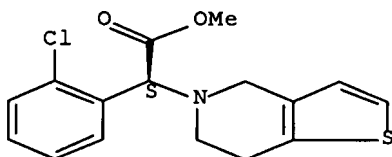
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004081015	A1	20040923	WO 2003-IN50	20030310
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003216707	A1	20040930	AU 2003-216707	20030310
IN 2003CN00583	A	20050415	IN 2003-CN583	20030421
US 2006100231	A1	20060511	US 2003-433210	20030530
PRIORITY APPLN. INFO.:			WO 2003-IN50	A 20030310
AB	A process for preparation of amorphous clopidogrel hydrogensulfate comprises: (A) dissolving clopidogrel in methanol, ethanol, or their mixts.; (B) adding concentrated sulfuric acid at approx. 0-50°; (C) refluxing the mixture for approx. 2 h; and (D) removing the solvent from the solution either by distillation, vacuum drying, or by spray drying.			
IC	ICM C07D495-04 ICS A61K031-44			
CC	63-6 (Pharmaceuticals) Section cross-reference(s): 28, 75			
IT	120202-66-6P , Clopidogrel hydrogen sulfate RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation) ; USES (Uses) (process for the preparation of amorphous clopidogrel hydrogensulfate)			
IT	113665-84-2 , Clopidogrel			

RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for the preparation of amorphous clopidogrel hydrogensulfate)
 IT 7664-93-9, Sulfuric acid, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for the preparation of amorphous clopidogrel hydrogensulfate using)
 IT 120202-66-6P, Clopidogrel hydrogen sulfate
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (process for the preparation of amorphous clopidogrel hydrogensulfate)
 RN 120202-66-6 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

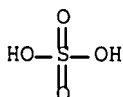
CRN 113665-84-2
 CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



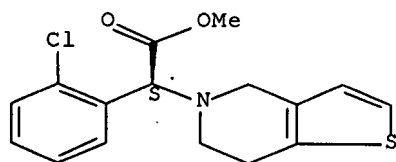
CM 2

CRN 7664-93-9
 CMF H2 O4 S

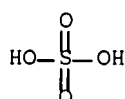


IT 113665-84-2, Clopidogrel
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for the preparation of amorphous clopidogrel hydrogensulfate)
 RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 7664-93-9, Sulfuric acid, reactions
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (process for the preparation of amorphous clopidogrel hydrogensulfate
 using)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 20 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:470987 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:42905

TITLE: Crystallization process for the preparation of the
 crystalline polymorphic form I of clopidogrel
 bisulfate

INVENTOR(S): Piechaczek, Janina; Serafin, Jadwiga; Maruszak,
 Wioleta; Balicki, Roman; Szelejewski, Wieslaw;
 Cybulski, Marcin; Maciejewski, Grzegorz; Wysoczynska,
 Maria; Glice, Magdalena; Korczak, Katarzyna

PATENT ASSIGNEE(S): Anpharm Przedsiębiorstwo Farmaceutyczne S.A., Pol.; et
 al.

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048385	A2	20040610	WO 2003-PL130	20031126
WO 2004048385	A3	20040805		
W: AL, AM, AT, AU, AZ, BA, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK,				
DM, EC, EE, ES, FI, GB, GD, GE, HR, HU, IL, IS, JP, KG, KR, KZ,				
LT, LU, LV, MA, MD, MK, MN, MW, MX, NI, NO, NZ, PT, RO, RU, SE,				
SK, SY, TJ, TM, TR, UA, US, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,				
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,				
SI, SK, TR				
AU 2003285841	A1	20040618	AU 2003-285841	20031126

PRIORITY APPLN. INFO.:

PL 2002-254427

A 20021128

WO 2003-PL130

W 20031126

AB The crystalline polymorphic form I of clopidogrel bisulfate is prepared by precipitating the salt formed in the neutralization reaction of the optically active base of clopidogrel, Me (S)-(+)- α -(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-5-acetate with concentrated sulfuric acid, using a precipitating solvent selected from aliphatic and cyclic ethers and iso-Bu Me ketone. An X-ray diffraction pattern of the title polymorphic compound is presented.

IC ICM C07D495-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 28, 75

IT **120202-66-6P**, Clopidogrel bisulfate

RL: PRP (Properties); SPN (Synthetic preparation); **PREP**
(Preparation)

(crystallization process for the preparation of the crystalline polymorphic form I of
clopidogrel bisulfate)

IT **7664-93-9**, Sulfuric acid, reactions **113665-84-2**,
Clopidogrel

RL: **RCT (Reactant); RACT (Reactant or reagent)**

(in a crystallization process for the preparation of the crystalline polymorphic form I
of clopidogrel bisulfate)

IT **120202-66-6P**, Clopidogrel bisulfate

RL: PRP (Properties); SPN (Synthetic preparation); **PREP**
(Preparation)

(crystallization process for the preparation of the crystalline polymorphic form I of
clopidogrel bisulfate)

RN 120202-66-6 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

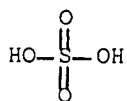
Absolute stereochemistry. Rotation (+).



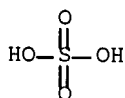
CM 2

CRN 7664-93-9

CMF H2 O4 S

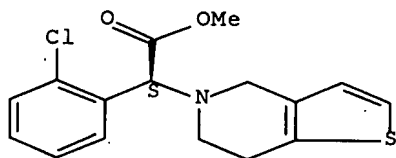


IT 7664-93-9, Sulfuric acid, reactions 113665-84-2,
 Clopidogrel
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (in a crystallization process for the preparation of the crystalline
 polymorphic form I
 of clopidogrel bisulfate)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
 dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L61 ANSWER 21 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:203837 ZCAPLUS Full-text
 DOCUMENT NUMBER: 140:241063
 TITLE: Method for the manufacture of crystalline form I of
 clopidogrel hydrogen sulfate
 INVENTOR(S): Veverka, Miroslav; Vodny, Stefan; Veverkova, Eva;
 Hajicek, Josef; Stepankova, Hana
 PATENT ASSIGNEE(S): Leciva, A.S., Czech Rep.
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004020443	A1	20040311	WO 2003-CZ49	20030826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CZ 297472	B6	20061213	CZ 2002-2906	20020827
CA 2495823	A1	20040311	CA 2003-2495823	20030826
AU 2003269673	A1	20040319	AU 2003-269673	20030826
EP 1554284	A1	20050720	EP 2003-750270	20030826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502238	T	20060119	JP 2004-569700	20030826
US 2006041136	A1	20060223	US 2005-525341	20050706
PRIORITY APPLN. INFO.:			CZ 2002-2906	A 20020827
			WO 2003-CZ49	W 20030826

AB A method for manufacturing the hydrogen sulfate (alpha S) of the alpha-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetic acid Me ester (i.e., clopidogrel hydrogen sulfate), in crystalline Form I, where the compound is separated out of a solution of clopidogrel in the form of the free base or salt in a solvent selected from the series of primary, secondary or tertiary C1-5 alcs. (e.g., 2-propanol), their esters with C1-4 carboxylic acids, or optionally of mixts. thereof.

IC ICM C07D495-04

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 28, 75

IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); **PREP (Preparation)**; PROC (Process)

(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate)

IT **7664-93-9**, Sulfuric acid, reactions **113665-84-2**, Clopidogrel

RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**

(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

IT **120202-66-6P**, Clopidogrel hydrogen sulfate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); **PREP (Preparation)**; PROC (Process)

(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate)

RN 120202-66-6 ZCAPLUS

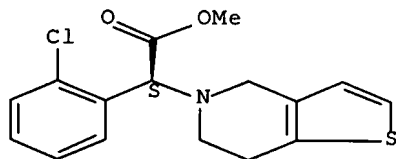
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

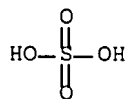
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



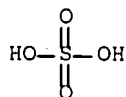
IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel

RL: **RCT (Reactant); RACT (Reactant or reagent)**

(method for the manufacture of crystalline form I of clopidogrel hydrogen sulfate using)

RN 7664-93-9 ZCAPLUS

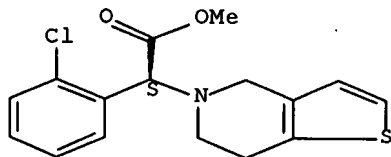
CN Sulfuric acid (CA INDEX NAME)



RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L61 ANSWER 22 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:310878 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:287712

TITLE: Racemization of optically active 2-substituted phenylglycine esters

INVENTOR(S): Maheshwari, Krishna K.; Sarma, Rayaprolu Kodandarama; Joshi, Shreerang Vidyadhar; Barde, Anup Ramkrishna; Sutar, Rajiv Pandurang; Ranade, Prasad Vasudeo

PATENT ASSIGNEE(S): USV Limited, India

SOURCE: U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004073057	A1	20040415	US 2002-271299	20021015
US 6812363	B2	20041102		
GB 2394473	A	20040428	GB 2003-24166	20031015
GB 2394473	B	20060315		
DE 10348674	A1	20040527	DE 2003-10348674	20031015
FR 2847579	A1	20040528	FR 2003-12059	20031015
			US 2002-271299	A 20021015

PRIORITY APPLN. INFO.:

AB A process for preparing a racemic mixture containing nearly equal amts. of stereo isomers of (2-chlorophenyl)glycine Me ester (I) involves heating an enantiomerically-enriched material with thionyl chloride. A useful enantiomer may thereby be recovered from unwanted mother liquors that would otherwise be discarded. In an example, 73.7 kg thionyl chloride was added to 100 kg (-)-I in 350 L methanol with stirring at 25-30°, the solution heated at reflux for about 12 h, and water added. Racemic I found in the organic layer was resolved, e.g., by the tartrate method.

IC ICM C07C229-38

INCL 560038000; 562401000

CC 34-2 (Amino Acids, Peptides, and Proteins)

IT **141109-14-0P**

RL: PUR (Purification or recovery); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT **141109-16-2P 212838-70-5P**

RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT **141109-13-9P 676132-76-6P 676132-77-7P 676132-78-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT **141109-17-3P 213018-92-9P**

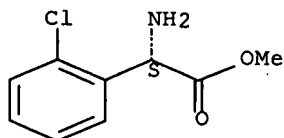
RL: SPN (Synthetic preparation); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via racemization/resolution)

IT **141109-14-0P**

RL: PUR (Purification or recovery); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via

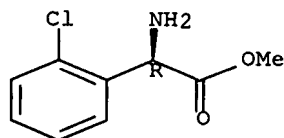
racemization/resolution)
RN 141109-14-0 ZCAPLUS
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



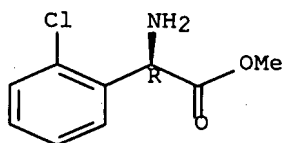
IT 141109-16-2P 212838-70-5P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation);
RACT (Reactant or reagent)
(recovery of useful isomer of (chlorophenyl)glycine ester via
racemization/resolution)
RN 141109-16-2 ZCAPLUS
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 212838-70-5 ZCAPLUS
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride,
(α R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



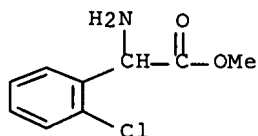
● HCl

IT 141109-13-9P 676132-76-6P 676132-77-7P
676132-78-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(recovery of useful isomer of (chlorophenyl)glycine ester via
racemization/resolution)

RN 141109-13-9 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME)



RN 676132-76-6 ZCAPLUS

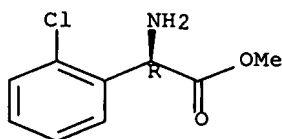
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-,
(2R,3R)-2,3-dihydroxybutanedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 141109-16-2

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (-).

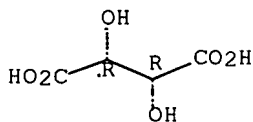


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



RN 676132-77-7 ZCAPLUS

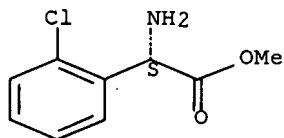
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-,
(2R,3R)-2,3-dihydroxybutanedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 141109-14-0

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (+).

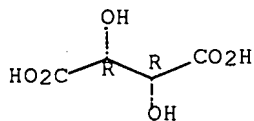


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



RN 676132-78-8 ZCAPLUS

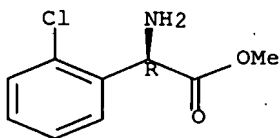
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-,
(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (9CI)
(CA INDEX NAME)

CM 1

CRN 141109-16-2

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (-).

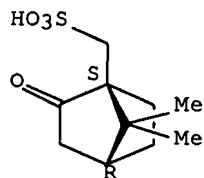


CM 2

CRN 3144-16-9

CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

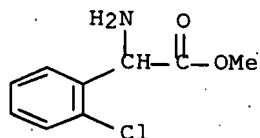


IT 141109-17-3P 213018-92-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(recovery of useful isomer of (chlorophenyl)glycine ester via
racemization/resolution)

RN 141109-17-3 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride
(9CI) (CA INDEX NAME)

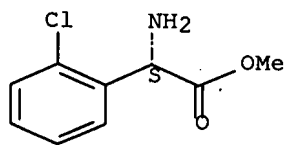


● HCl

RN 213018-92-9 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride,
(α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 23 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:838194 ZCAPLUS Full-text

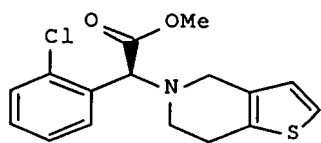
DOCUMENT NUMBER: 146:441665

TITLE: Preparation of clopidogrel

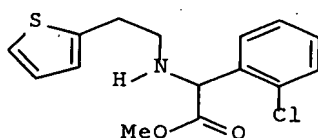
INVENTOR(S): Bhushan, Lohray Vidya; Bhushan, Lohray Braj; Bipin,
Pandey

PATENT ASSIGNEE(S): Zydus Research Center, Cadila Health Care Ltd., India
 SOURCE: Indian, 33pp.
 CODEN: INXXAP
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 193668	A1	20040731	IN 2001-MU335	20010411
IN 2003MU01007	A	20050715	IN 2003-MU1007	20030924
IN 2003MU01008	A	20050715	IN 2003-MU1008	20030924
PRIORITY APPLN. INFO.: GI			IN 2001-MU335	A3 20010411



I



II

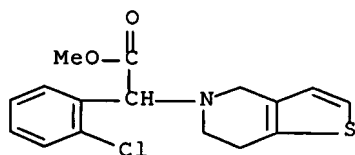
- AB A process for the preparation of title compound I and its pharmaceutically acceptable salts was disclosed. For example, 1,3-dioxalane/HCL mediated cyclization of amine II hydrochloride afforded the racemate of clopidogrel in 95% yield.
- IC ICM A61K031-44
ICS C07D495-04
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- IT **90055-48-4P 113665-84-2P**, S-Clopidogrel
120202-66-6P 120202-69-9P 120202-71-3P
135046-48-9P 934504-75-3P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**;
 USES (Uses)
 (preparation of clopidogrel)
- IT 67-56-1, Methanol, reactions 937-14-4, Mcpba 1333-74-0, Hydrogen, reactions 1504-71-8 4648-54-8, Trimethylsilyl azide **7664-93-9**, Sulfuric acid, reactions 7719-09-7, Thionyl chloride 20762-60-1, Potassium azide 26628-22-8, Sodium azide 40412-06-4, 2-Thiophene ethanol tosylate 934504-65-1
 RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
 (preparation of clopidogrel)
- IT 3380-96-9P **141109-13-9P 141109-14-0P**
141109-16-2P 934504-66-2P 934504-67-3P 934504-68-4P
 934504-72-0P 934504-73-1P 934504-74-2P
 RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; **RACT (Reactant or reagent)**
 (preparation of clopidogrel)
- IT **90055-48-4P 113665-84-2P**, S-Clopidogrel
120202-66-6P 120202-69-9P 120202-71-3P
135046-48-9P 934504-75-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(preparation of clopidogrel)

RN 90055-48-4 ZCAPLUS

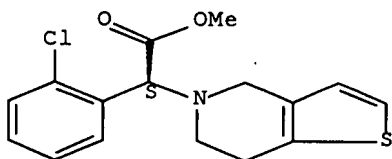
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester (CA INDEX NAME)



RN 113665-84-2 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 120202-66-6 ZCAPLUS

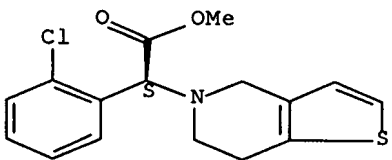
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

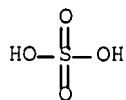
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

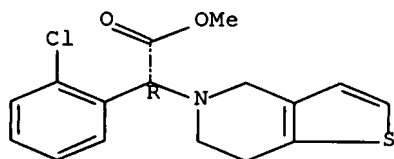
CMF H2 O4 S



RN 120202-69-9 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 120202-71-3 ZCAPLUS

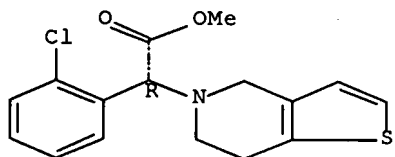
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α R)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 120202-69-9

CMF C16 H16 Cl N O2 S

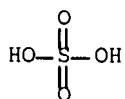
Absolute stereochemistry. Rotation (-).



CM 2

CRN 7664-93-9

CMF H2 O4 S



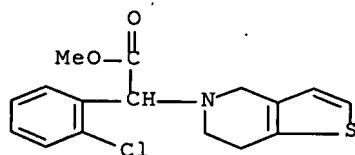
RN 135046-48-9 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 90055-48-4

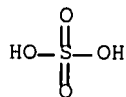
CMF C16 H16 Cl N O2 S



CM 2

CRN 7664-93-9

CMF H2 O4 S



RN 934504-75-3 ZCAPLUS

CN INDEX NAME NOT YET ASSIGNED

CM 1

CRN 113665-84-2

CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).

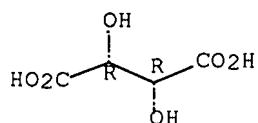


CM 2

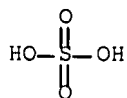
CRN 87-69-4

CMF C4 H6 O6

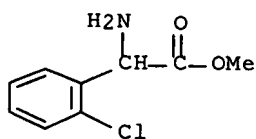
Absolute stereochemistry.



IT 7664-93-9, Sulfuric acid, reactions
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(preparation of clopidogrel)
RN 7664-93-9 ZCAPLUS
CN Sulfuric acid (CA INDEX NAME)

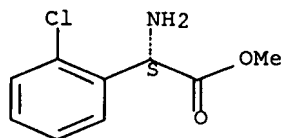


IT 141109-13-9P 141109-14-0P 141109-16-2P
RL: **RCT (Reactant); SPN (Synthetic preparation); PREP**
(Preparation); **RACT (Reactant or reagent)**
(preparation of clopidogrel)
RN 141109-13-9 ZCAPLUS
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME)



RN 141109-14-0 ZCAPLUS
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-
(CA INDEX NAME)

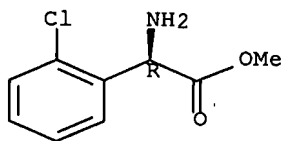
Absolute stereochemistry. Rotation (+).



RN 141109-16-2 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 24 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:370683 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:380607

TITLE: Preparation of clopidogrel salts with alkyl-sulphuric acids

INVENTOR(S): Castaldi, Graziano; Bologna, Alberto; Magrone, Domenico

PATENT ASSIGNEE(S): Dinamite Dipharma S.P.A. (In Abbreviated Form Dipharma S.P.A.), Italy

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

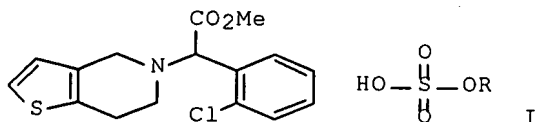
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

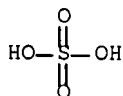
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1415993	A1	20040506	EP 2003-23023	20031013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004132765	A1	20040708	US 2003-686666	20031017
PRIORITY APPLN. INFO.:			IT 2002-MI2228	A 20021021
OTHER SOURCE(S):	MARPAT 140:380607			
GI				



AB Clopidogrel salts with alkyl-sulfuric acids, having formula I wherein R is a straight or branched C1-C10 alkyl group; preparation thereof and the industrial and therapeutical use thereof are disclosed. A reactor was loaded at room temperature with clopidogrel hemisulfate (50 g, 0.12 mol) and isopropanol (500 mL) and refluxed under stirring. After about 5 h, the reaction mixture was cooled to room temperature and the product precipitated

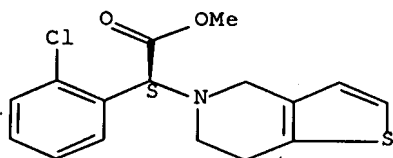
after approx. 3 h. The solid was filtered after about 15 h and dried under vacuum (200 mm Hg) at a temperature of 60°C for 24 h to obtain clopidogrel iso-Pr sulfate: yield = 88.8%, m.p. 167.1°C, and purity >99.9%.

IC ICM C07D495-04
 ICS A61K031-4365; A61P007-02; C07D333-00; C07D221-00
 CC 63-5 (Pharmaceuticals)
 IT 67-63-0, Isopropanol, reactions 78-92-2, sec-Butanol 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (clopidogrel salts with alkyl-sulfuric acids)
 IT 120202-66-6P, ClopiDogrel hemisulfate
 RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
 (clopidogrel salts with alkyl-sulfuric acids)
 IT 7664-93-9, Sulfuric acid, reactions 113665-84-2, Clopidogrel
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (clopidogrel salts with alkyl-sulfuric acids)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



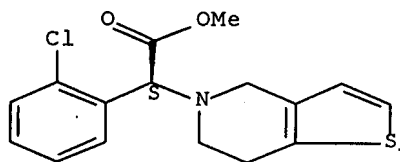
RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (αS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 120202-66-6P, ClopiDogrel hemisulfate
 RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
 (clopidogrel salts with alkyl-sulfuric acids)
 RN 120202-66-6 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-dihydro-, methyl ester, (αS)-, sulfate (1:1) (CA INDEX NAME)
 CM 1
 CRN 113665-84-2
 CMF C16 H16 Cl N O2 S

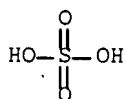
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

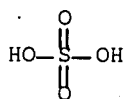
L61 ANSWER 25 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:892782 ZCAPLUS Full-text
 DOCUMENT NUMBER: 139:364917
 TITLE: A process for the preparation of clopidogrel
 INVENTOR(S): Castaldi, Graziano; Barreca, Giuseppe; Bologna, Alberto
 PATENT ASSIGNEE(S): Dinamite Dipharma S.p.A., Italy
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093276	A1	20031113	WO 2003-EP4179	20030422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI0933	A1	20031103	IT 2002-MI933	20020503
CA 2485070	A1	20031113	CA 2003-2485070	20030422
AU 2003224115	A1	20031117	AU 2003-224115	20030422
EP 1501838	A1	20050202	EP 2003-720514	20030422

EP 1501838 B1 20070411
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 2005143414 A1 20050630 US 2003-513156 20030422
 CN 1649877 A 20050803 CN 2003-809967 20030422
 JP 2005530757 T 20051013 JP 2004-501415 20030422
 PRIORITY APPLN. INFO.: IT 2002-MI933 A 20020503
 WO 2003-EP4179 W 20030422

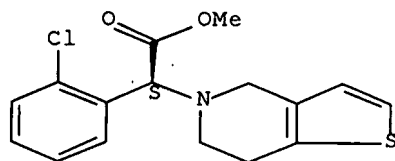
OTHER SOURCE(S): CASREACT 139:364917; MARPAT 139:364917

AB A process for the preparation of clopidogrel by the condensation reaction of N,N'-bis(4,5,6,7-tetrahydro[3,2-c]thienopyridyl)methane with C1-4 alkyl (2R)-(2-chlorophenyl)-2-haloacetates or alkyl (2R)-2-(2-chlorophenyl)-2-(substituted sulfonyloxy)acetates [e.g., Me (2R)-2-(2-chlorophenyl)-2-(4-nitrobenzenesulfonyloxy)acetate].
 IC ICM C07D495-04
 ICS C07D519-00; A61K031-4365; A61P009-00; C07D333-00; C07D221-00; C07D495-00
 CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 45
 IT 7664-93-9, Sulfuric acid, reactions 223123-80-6 622835-93-2
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (in a process for the preparation of clopidogrel)
 IT 113665-84-2P, Clopidogrel
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (process for the preparation of clopidogrel)
 IT 120202-66-6P, Clopidogrel hemisulfate
 RL: SPN (Synthetic preparation); **PREP (Preparation)**
 (process for the preparation of clopidogrel)
 IT 7664-93-9, Sulfuric acid, reactions
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (in a process for the preparation of clopidogrel)
 RN 7664-93-9 ZCAPLUS
 CN Sulfuric acid (CA INDEX NAME)



IT 113665-84-2P, Clopidogrel
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (process for the preparation of clopidogrel)
 RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

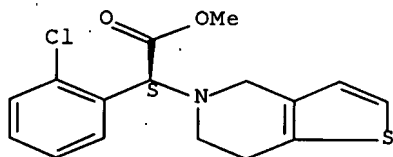


IT 120202-66-6P, Clopidogrel hemisulfate
 RL: SPN (Synthetic preparation); **PREP (Preparation)**
 (process for the preparation of clopidogrel)
 RN 120202-66-6 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α-(2-chlorophenyl)-6,7-
 dihydro-, methyl ester, (αS)-, sulfate (1:1) (CA INDEX NAME)

CM 1

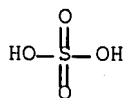
CRN 113665-84-2
 CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
 CMF H2 O4 S



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 26 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:473265 ZCAPLUS Full-text
 DOCUMENT NUMBER: 139:41853
 TITLE: preparation of crystal and amorphous forms of
 clopidogrel hydrogen sulfate for pharmaceuticals
 INVENTOR(S): Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Wize,
 Shlomit; Maydan, Sharon Avhar; Lidor-Hadas, Rami
 PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003114479	A1	20030619	US 2002-74409	20020212
US 6767913	B2	20040727		
CA 2470479	A1	20030626	CA 2002-2470479	20021218
WO 2003051362	A2	20030626	WO 2002-US40679	20021218
WO 2003051362	A3	20030807		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002366383	A1	20030630	AU 2002-366383	20021218
EP 1467735	A2	20041020	EP 2002-805215	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
HU 200402485	A2	20050428	HU 2004-2485	20021218
JP 2005514387	T	20050519	JP 2003-552295	20021218
CN 1620293	A	20050525	CN 2002-828204	20021218
CN 1923835	A	20070307	CN 2006-10139532	20021218
US 2003225129	A1	20031204	US 2003-339008	20030108
US 7074928	B2	20060711		
ZA 2004004733	A	20050615	ZA 2004-4733	20040615
NO 2004003038	A	20040909	NO 2004-3038	20040716

PRIORITY APPLN. INFO.:

US 2001-342440P	P	20011218
US 2001-342351P	P	20011221
US 2002-348182P	P	20020111
US 2002-74409	A	20020212
US 2002-359157P	P	20020221
CN 2002-828204	A3	20021218
WO 2002-US40679	W	20021218

AB The present invention provides new crystalline forms III, IV and V of clopidogrel hydrogen sulfate and the amorphous form of clopidogrel hydrogen sulfate, as well as their pharmaceutical compns., and method of treatments with such compns. The present invention further provides a novel process where the amorphous form is converted to Form I by contacting Form I with an ether. Clopidogrel hydrogen sulfate (2 g) was dissolved in MeOH (4 mL). The resulting solution was added dropwise to di-Et ether (350 mL). The suspension was stirred at room temperature for 45 min. The solid was filtered and dried at about 50° in a vacuum oven for 24 h to give 1.12 g (56%) of clopidogrel hydrogen sulfate, which characterization data showed to be the amorphous form.

IC ICM C07D498-02

ICS A61K031-4743

INCL 514301000; 546114000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 28, 75

IT 120202-66-6P, Clopidogrel hydrogen sulfate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 7664-93-9, Sulfuric acid, reactions
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 113665-84-2, Clopidogrel
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

IT 120202-66-6P, Clopidogrel hydrogen sulfate
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
 (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

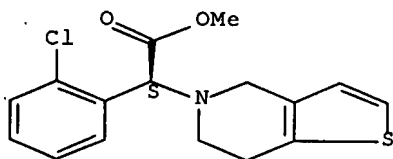
RN 120202-66-6 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (1:1) (CA INDEX NAME)

CM 1

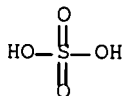
CRN 113665-84-2
 CMF C16 H16 Cl N O2 S

Absolute stereochemistry. Rotation (+).



CM 2

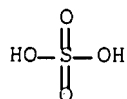
CRN 7664-93-9
 CMF H2 O4 S



IT 7664-93-9, Sulfuric acid, reactions
 RL: **RCT (Reactant); RACT (Reactant or reagent)**
 (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate for pharmaceuticals)

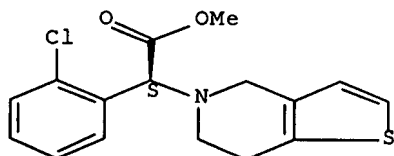
RN 7664-93-9 ZCAPLUS

CN Sulfuric acid (CA INDEX NAME)



IT **113665-84-2**, Clopidogrel
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
 (Reactant or reagent); USES (Uses)
 (preparation of crystal and amorphous forms of clopidogrel hydrogen sulfate
 for pharmaceuticals)
 RN 113665-84-2 ZCAPLUS
 CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
 dihydro-, methyl ester, (α S)- (CA INDEX NAME) -

Absolute stereochemistry. Rotation (+).

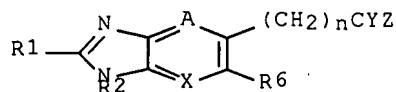


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 27 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:51438 ZCAPLUS Full-text
 DOCUMENT NUMBER: 136:118447
 TITLE: Preparation of benzimidazolecarboxylates and related
 compounds as viral polymerase inhibitors
 INVENTOR(S): Beaulieu, Pierre Louis; Fazal, Gulrez; Gillard, James;
 Kukolj, George; Austel, Volkhard
 PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
 SOURCE: PCT Int. Appl., 322 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004425	A2	20020117	WO 2001-CA989	20010704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002065418	A1	20020530	US 2001-898297	20010703

US 6448281	B2	20020910		
CA 2412718	A1	20020117	CA 2001-2412718	20010704
EP 1301487	A2	20030416	EP 2001-951274	20010704
EP 1301487	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502761	T	20040129	JP 2002-509292	20010704
AT 346049	T	20061215	AT 2001-951274	20010704
US 6479508	B1	20021112	US 2001-995099	20011127
CA 2439176	A1	20020912	CA 2002-2439176	20020306
WO 2002070739	A2	20020912	WO 2002-CA323	20020306
WO 2002070739	A3	20030530		
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AU 2002244566	A1	20020919	AU 2002-244566	20020306
EP 1370682	A2	20031217	EP 2002-712681	20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200400039	A2	20040428	HU 2004-39	20020306
JP 2004520839	T	20040715	JP 2002-570761	20020306
NZ 528644	A	20050527	NZ 2002-528644	20020306
US 2003232816	A1	20031218	US 2002-238282	20020910
US 6794404	B2	20040921		
US 2004110126	A1	20040610	US 2004-471164	20040205
US 2004224955	A1	20041111	US 2004-851710	20040521
PRIORITY APPLN. INFO.:				
			US 2000-216084P	P 20000706
			US 2001-274374P	P 20010308
			US 2001-281343P	P 20010405
			US 2001-898297	A3 20010703
			WO 2001-CA989	W 20010704
			US 2001-995099	A3 20011127
			WO 2002-CA323	W 20020306
			US 2002-238282	A1 20020910
OTHER SOURCE(S): MARPAT 136:118447				
GI				



AB Title compds. [I; X = CH, N; Y = O, S; Z = OH, NH₂, NMeR₃, NHR₃, OR₃, 5-6 membered (substituted) heterocyclyl; A = N, COR₇, CR₅; R₅ = H, halo, alkyl; R₇ = H, alkyl; X and A are not both N; R₆ = H, halo, alkyl, OR₇; R₇ = H, alkyl; R₁ = (substituted) hetero(bi)cyclyl, Ph, phenylalkyl, alkenyl, phenylalkenyl, cycloalkyl, alkyl, CF₃; R₂ = (substituted) alkyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, adamantyl, Ph, pyridyl; R₃ = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, alkenyl, cycloalkylalkenyl, arylalkenyl,

dialkylamino, heterocyclyl, etc.; n = 0, 1], were prepared Thus, Me 3-amino-4-cyclohexylaminobenzoate (preparation given), 2-pyridinecarboxaldehyde, and Oxone were stirred in DMF to give 80% Et 1-cyclohexyl-2-pyridin-2-yl-1H-benzimidazole-5-carboxylate, which was saponified with aqueous NaOH in MeOH to give 91% 1-cyclohexyl-2-pyridin-2-yl- 1H-benzimidazole-5-carboxylic acid. The latter inhibited hepatitis C virus RNA dependent polymerase (NS5B) with IC50 = 1-5 µM.

IC ICM C07D235-00

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 34

IT 120-57-0P, Piperonal 400-94-2P 2439-68-1P 5292-43-3P, tert-Butyl
bromoacetate 7499-07-2P 13226-99-8P 16588-16-2P 19367-38-5P
20866-48-2P 24015-98-3P 42718-19-4P 71787-35-4P 86068-94-2P
86937-05-5P 87815-77-8P 91252-27-6P 104174-57-4P 104338-21-8P
107146-41-8P 109431-87-0P 113850-71-8P 129960-90-3P
141109-17-3P 171738-42-4P 179232-29-2P 190367-56-7P
190367-57-8P 203736-17-8P 211186-22-0P 327051-33-2P 347174-05-4P
390815-31-3P 390815-32-4P 390815-33-5P 390815-34-6P 390815-35-7P
390815-36-8P 390815-37-9P 390815-38-0P 390815-39-1P 390815-40-4P
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390815-46-0P 390815-47-1P 390815-48-2P 390815-49-3P 390815-50-6P
390815-51-7P 390815-53-9P 390815-54-0P 390815-55-1P 390815-56-2P
390815-57-3P 390815-58-4P 390815-59-5P 390815-60-8P 390815-61-9P
390815-62-0P 390815-63-1P 390815-64-2P 390815-65-3P 390815-66-4P
390815-67-5P 390815-68-6P 390815-69-7P 390815-70-0P 390815-71-1P
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390816-08-7P 390816-09-8P 390816-10-1P 390816-11-2P 390816-12-3P
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390816-44-1P 390816-45-2P 390816-46-3P 390816-47-4P 390816-48-5P
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390816-61-2P 390816-62-3P 391612-31-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzimidazolecarboxylates and related compds. as viral polymerase inhibitors)

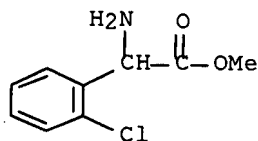
IT **141109-17-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzimidazolecarboxylates and related compds. as viral polymerase inhibitors)

RN 141109-17-3 ZCAPLUS

CN Benzeneacetic acid, α-amino-2-chloro-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L61 ANSWER 28 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:823424 ZCAPLUS Full-text

DOCUMENT NUMBER: 139:6655

TITLE: Highly potent inhibitors of TNF- α production.
Part I. Discovery of new chemical leads and Their
structure-Activity relationships

AUTHOR(S): Matsui, Toshiaki; Kondo, Takashi; Nishita, Yoshitaka;
Itadani, Satoshi; Nakatani, Shingo; Omawari,
Nagashige; Sakai, Masaru; Nakazawa, Shuichi; Ogata,
Akihito; Mori, Hideaki; Terai, Kouichiro; Kamoshima,
Wataru; Ohno, Hiroyuki; Obata, Takaaki; Nakai, Hisao;
Toda, Masaaki

CORPORATE SOURCE: Fukui Research Institute, Ono Pharmaceutical Co.,
Ltd.; Sakai, Fukui, 913-8638, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(12),
3757-3786

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:6655

AB Discovery of new chemical leads of inhibitors for TNF- α production starting
from the chemical modification of 2-(octanoylamino)-2-phenylethyl disodium
phosphate (I) is reported. Further biol. studies of I to disclose the site of
its action strongly suggested that I inhibits LPS-induced TNF- α expression in
the liver and spleen of mice. Structure-activity relationships (SARs) are also
discussed and full details including the chemical are reported.

CC 25-22 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

IT 75-03-6, Ethyl iodide 75-36-5, Acetyl chloride 98-88-4, Benzoyl
chloride 99-66-1, 2-Propylpentanoic acid 107-30-2, Chloromethyl methyl
ether 109-02-4, N-Methylmorpholine 111-64-8, Octanoyl chloride
112-38-9, 10-Undecenoic acid 141-75-3, Butanoyl chloride 142-61-0,
Hexanoyl chloride 288-32-4, Imidazole, reactions 542-69-8, n-Butyl
iodide 558-17-8, tert-Butyl iodide 620-05-3, Benzyl iodide 626-20-0
628-17-1, n-Pentyl iodide 638-45-9, n-Hexyl iodide 937-14-4,
m-Chloroperbenzoic acid 1556-18-9, Cyclopentyl iodide 1809-05-8,
Pentane, 3-iodo- 2270-20-4, Benzenepentanoic acid 2525-62-4, Hexyl
isocyanate 2528-61-2, Heptanoyl chloride 2919-23-5, Cyclobutyl alcohol
5416-03-5, Pentylloxycetic acid 6092-54-2, Hexyl chloroformate
7795-95-1, 1-Octanesulfonyl chloride 17701-32-5 18162-48-6,
tert-Butyldimethylsilyl chloride 22683-44-9, Pentylthioacetic acid
38557-29-8, Cyclobutyl iodide 41639-57-0 41639-61-6, 6-Methoxyhexanoic
acid 43152-88-1 43189-19-1 43189-20-4 43189-24-8 54011-37-9
55243-15-7 56613-80-0 58148-20-2 70160-06-4, 5-Ethoxypentanoic acid
70946-42-8 73664-43-4, n,N-Dimethyl-2-iodoacetamide 74273-47-5

77651-55-9 102690-88-0 108549-23-1, Dibenzyl
 diisopropylphosphoramidite 117049-14-6 138891-55-1 **141109-13-9**
 179814-89-2 289052-50-2 526217-34-5 532986-35-9 532986-37-1
 532986-51-9 532986-70-2 532987-04-5 532987-11-4 532987-12-5
 532987-13-6 532987-14-7 532987-18-1

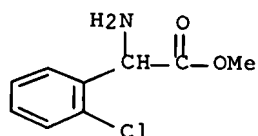
RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of alkylamino aryl disodium phosphates and their
 structure-activity relationships as highly potent inhibitors of
 TNF- α production)

IT **141109-13-9**

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of alkylamino aryl disodium phosphates and their
 structure-activity relationships as highly potent inhibitors of
 TNF- α production)

RN 141109-13-9 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME).

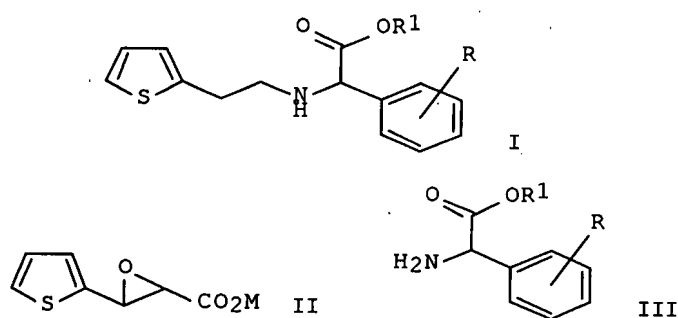


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 29 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:612091 ZCAPLUS Full-text
 DOCUMENT NUMBER: 129:245036
 TITLE: Improved method for preparing 2-thienylethylamine
 derivatives, including an intermediate for clopidogrel
 INVENTOR(S): Castro, Bertrand; Dormoy, Jean-Robert; Previero, Aldo
 PATENT ASSIGNEE(S): Sanofi, Fr.
 SOURCE: PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839322	A1	19980911	WO 1998-FR441	19980305
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
FR 2760456	A1	19980911	FR 1997-2621	19970305
FR 2760456	B1	20000512		
CA 2283126	A1	19980911	CA 1998-2283126	19980305
AU 9868394	A	19980922	AU 1998-68394	19980305

EP 971915	A1	20000119	EP 1998-913841	19980305
EP 971915	B1	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808174	A	20000516	BR 1998-8174	19980305
JP 2001513806	T	20010904	JP 1998-538240	19980305
AT 240311	T	20030515	AT 1998-913841	19980305
ES 2200332	T3	20040301	ES 1998-913841	19980305
US 6080875	A	20000627	US 1999-380450	19990902
MX 9908089	A	20000630	MX 1999-8089	19990902
NO 9904304	A	19991103	NO 1999-4304	19990903
PRIORITY APPLN. INFO.:			FR 1997-2621	A 19970305
			WO 1998-FR441	W 19980305
OTHER SOURCE(S):			CASREACT 129:245036; MARPAT 129:245036	
GI				



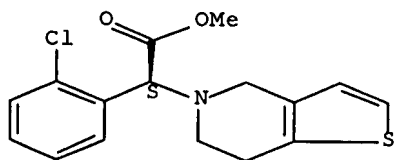
- AB The invention concerns a method for preparing 2-thienylethylamine derivs. I [R = halo; R1 = C1-4 alkyl, preferably Me] and their acid addition salts. The process involves reaction of a thienylglycidic acid derivative II [M = alkali metal, or alkaline earth metal fraction] with a phenylglycine ester III or its strong acid addition salt, in the presence of an alkali metal borohydride X-Y [in which X = alkali metal atom; Y = BH₃CN or BH(4-w)Zw; Z = carboxylic acid radical; w = 1, 2, 3] and optionally in the presence of a C1-C4 carboxylic acid, and followed optionally by conversion to an acid addition salt. For instance, reaction of II [M = Na] with (+)-(S)-III.HCl [R = 2-Cl; R1 = Me] and NaBH₃CN in MeOH in the presence of AcOH at 18° gave, after workup and acidification with HCl in MeOH, title compound (+)-(S)-I.HCl [R = 2-Cl; R1 = Me] (IV) in 75% isolated yield. Preps. of the corresponding starting materials II and III are described. IV is an important intermediate for the platelet antiaggregant and antithrombotic drug clopidogrel.
- IC ICM C07D333-20
- CC 27-8 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 45, 63
- IT **113665-84-2P**, Clopidogrel
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(intermediate for; improved preparation of thienylethylamine derivs.)
- IT **141109-14-0P**, (+)-(S)-Methyl α-amino-α-(2-chlorophenyl)acetate **213018-92-9P**, (+)-(S)-Methyl α-amino-α-(2-chlorophenyl)acetate hydrochloride
RL: IMF (Industrial manufacture); PUR (Purification or recovery); **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**;

RACT (Reactant or reagent)

(invention starting material; improved preparation of thienylethylamine derivs.)

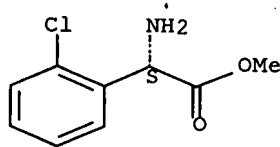
- IT 88744-36-9P, (R,S)- α -Amino- α -(2-chlorophenyl)acetic acid
141109-17-3P, (R,S)-Methyl α -amino- α -(2-chlorophenyl)acetate hydrochloride **212967-33-4P**, (S)-Methyl α -amino- α -(2-chlorophenyl)acetate (-)-N-(2,4-dinitrobenzoyl)phenylglycine salt
RL: IMF (Industrial manufacture); **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(precursor; improved preparation of thienylethylamine derivs.)
- IT **113665-84-2P**, Clopidogrel
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(intermediate for; improved preparation of thienylethylamine derivs.)
- RN 113665-84-2 ZCAPLUS
- CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



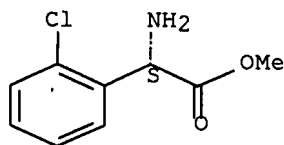
- IT **141109-14-0P**, (+)-(S)-Methyl α -amino- α -(2-chlorophenyl)acetate **213018-92-9P**, (+)-(S)-Methyl α -amino- α -(2-chlorophenyl)acetate hydrochloride
RL: IMF (Industrial manufacture); PUR (Purification or recovery); **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(invention starting material; improved preparation of thienylethylamine derivs.)
- RN 141109-14-0 ZCAPLUS
- CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



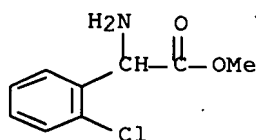
- RN 213018-92-9 ZCAPLUS
- CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

IT **141109-17-3P**, (R,S)-Methyl α -amino- α -(2-chlorophenyl)acetate hydrochloride **212967-33-4P**, (S)-Methyl α -amino- α -(2-chlorophenyl)acetate (-)-N-(2,4-dinitrobenzoyl)phenylglycine salt
 RL: IMF (Industrial manufacture); **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)** (precursor; improved preparation of thienylethylamine derivs.)
 RN 141109-17-3 ZCAPLUS
 CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

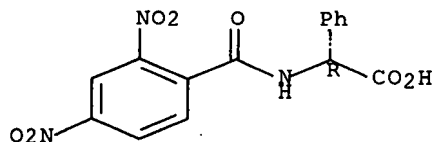
RN 212967-33-4 ZCAPLUS
 CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-, (α R)- α -[(2,4-dinitrobenzoyl)amino]benzeneacetate (9CI) (CA INDEX NAME)

CM 1

CRN 212967-32-3

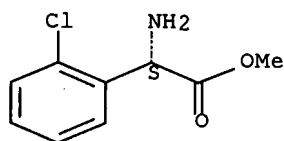
CMF C15 H11 N3 O7

Absolute stereochemistry. Rotation (-).



CRN 141109-14-0
CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 30 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:612064 ZCAPLUS Full-text

DOCUMENT NUMBER: 129:231012

TITLE: Method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts

INVENTOR(S): Castro, Bertrand; Previero, Aldo

PATENT ASSIGNEE(S): Sanofi, Fr.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839286	A1	19980911	WO 1998-FR406	19980302
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2760452	A1	19980911	FR 1997-2618	19970305
FR 2760452	B1	19990528		
AU 9867363	A	19980922	AU 1998-67363	19980302
PRIORITY APPLN. INFO.:			FR 1997-2618	A 19970305
			WO 1998-FR406	W 19980302

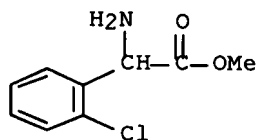
OTHER SOURCE(S): MARPAT 129:231012

AB Enantiomeric α -amino acid esters $\text{RC}_6\text{H}_4\text{CH}(\text{NH}_2)\text{CO}_2\text{R}_1$ (R = H, halo, OH, alkyl, alkoxy; R_1 = alkyl, alkenyl, benzyl) were obtained from the opposite enantiomer or the racemate via diastereoisomeric salts. Thus, treatment of DL-phenylglycine Me ester hydrochloride with N-acetyl-L-phenylglycine in MeOH containing KOAc afforded D-phenylglycine Me ester N-acetyl-L-phenylglycinate, which was hydrolyzed by aqueous sodium carbonate to give D-phenylglycine Me ester hydrochloride.

IC ICM C07C227-34

ICS C07C227-36; C07C233-47; C07C229-36; C07B057-00

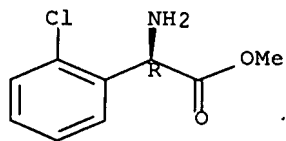
CC 34-2 (Amino Acids, Peptides, and Proteins)
 IT 15028-40-7P 43189-12-4P **141109-17-3P**
 RL: PUR (Purification or recovery); PREP (Preparation)
 (method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)
 IT 212779-53-8P 212779-54-9P 212779-55-0P 212779-56-1P 212779-57-2P
 212779-74-3P **212838-69-2P 212838-72-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)
 IT 15028-39-4P 19883-41-1P 24461-61-8P 26531-82-8P 37760-98-8P
 37763-23-8P **212838-70-5P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)
 IT **141109-17-3P**
 RL: PUR (Purification or recovery); PREP (Preparation)
 (method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)
 RN 141109-17-3 ZCAPLUS
 CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **212838-69-2P 212838-72-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)
 RN 212838-69-2 ZCAPLUS
 CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-, (α S)- α -[(3,5-dinitrobenzoyl)amino]benzeneacetate (9CI) (CA INDEX NAME)
 CM 1
 CRN 141109-16-2
 CMF C9 H10 Cl N O2

. Absolute stereochemistry. Rotation (-).

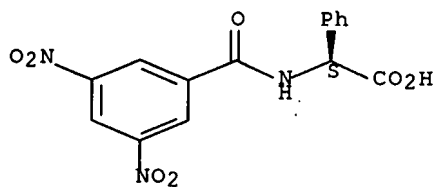


CM 2

CRN 90761-62-9

CMF C15 H11 N3 O7

Absolute stereochemistry. Rotation (+).



RN 212838-72-7 ZCAPLUS

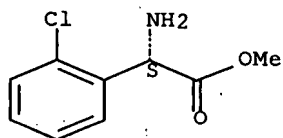
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-,
(α R)- α -[(3,5-dinitrobenzoyl)amino]benzeneacetate (9CI) (CA
INDEX NAME)

CM 1

CRN 141109-14-0

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (+).

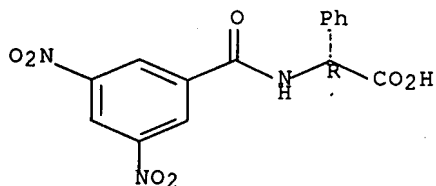


CM 2

CRN 74927-72-3

CMF C15 H11 N3 O7

Absolute stereochemistry. Rotation (-).



IT 212838-70-5P

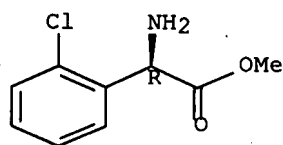
RL: SPN (Synthetic preparation); PREP (Preparation)

(method for obtaining α -amino acid enantiomers and intermediate diastereoisomeric salts)

RN 212838-70-5 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride, (α R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 31 OF 31 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:490266 ZCAPLUS Full-text

DOCUMENT NUMBER: 117:90266

TITLE: Preparation of methyl α -[4,5,6,7-tetrahydrothieno[3,2-c]pyrid-5-yl]-2'-chlorophenylacetate

INVENTOR(S): Descamps, Marcel; Radisson, Joel

PATENT ASSIGNEE(S): Sanofi SA, Fr.

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 466569	A1	19920115	EP 1991-401891	19910708
EP 466569	B1	19960417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2664596	A1	19920117	FR 1990-8749	19900710
FR 2664596	B1	19940610		
AU 9179492	A	19920116	AU 1991-79492	19910702

AU 645816	B2	19940127		
US 5204469	A	19930420	US 1991-725650	19910703
CA 2046482	A1	19920111	CA 1991-2046482	19910708
CA 2046482	C	20011030		
AT 136899	T	19960515	AT 1991-401891	19910708
ES 2086505	T3	19960701	ES 1991-401891	19910708
PL 172216	B1	19970829	PL 1991-290980	19910708
JP 04230387	A	19920819	JP 1991-168086	19910709
JP 2945174	B2	19990906		
HU 61556	A2	19930128	HU 1991-2311	19910709
HU 215957	B	19990329		
KR 198503	B1	19990615	KR 1991-11791	19910709
PRIORITY APPLN. INFO.:			FR 1990-8749	A 19900710

AB The title compound (I) was prepared Thus, 2-ClC₆H₄CH(NH₂)CO₂Me (preparation from acid given) was condensed with RCH₂CH₂OSO₂C₆H₄Me-4 (R = 2-thienyl) and the product treated with (+)-camphor-10-sulfonic acid to give, after decomposition of the precipitated salt, (+)-2-ClC₆H₄CH(CO₂Me)NHCH₂CH₂R (R as above) which was cyclocondensed with HCHO to give (+)-I.HCl (clopidogrel) a known antithrombotic agent.

IC ICM C07D495-04
ICS C07D333-20; A61K031-435

ICI C07D495-04, C07D333-00, C07D221-00

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT **141109-15-1P** 141109-21-9P 141109-22-0P 141315-51-7P
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation and decomposition of, in preparation of thienopyridyl(chlorophenyl)acetate)

IT 90055-47-3P **141109-13-9P 141109-14-0P 141109-16-2P 141109-17-3P** 141109-18-4P 141109-19-5P 141109-20-8P 141109-24-2P 141109-26-4P
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation and reaction of, in preparation of thienopyridyl(chlorophenyl)acetate)

IT **120202-65-5P 130209-90-4P 141196-65-8P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)

IT **141109-15-1P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(preparation and decomposition of, in preparation of thienopyridyl(chlorophenyl)acetate)

RN 141109-15-1 ZCAPLUS

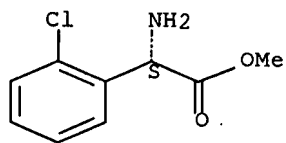
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 141109-14-0

CMF C9 H10 Cl N O2

Absolute stereochemistry. Rotation (+).

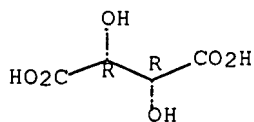


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



IT 141109-13-9P 141109-14-0P 141109-16-2P

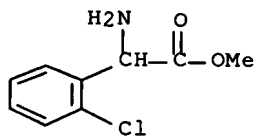
141109-17-3P

RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**

(preparation and reaction of, in preparation of thienopyridyl(chlorophenyl)acetate)

RN 141109-13-9 ZCAPLUS

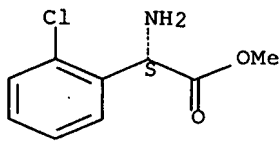
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester (CA INDEX NAME)



RN 141109-14-0 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α S)- (CA INDEX NAME)

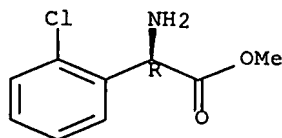
Absolute stereochemistry. Rotation (+).



RN 141109-16-2 ZCAPLUS

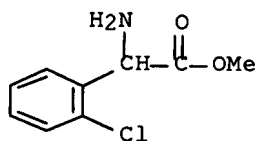
CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, (α R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 141109-17-3 ZCAPLUS

CN Benzeneacetic acid, α -amino-2-chloro-, methyl ester, hydrochloride
(9CI) (CA INDEX NAME)



● HCl

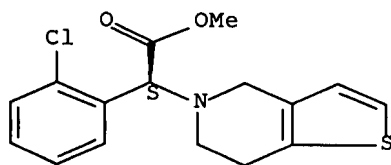
IT 120202-65-5P 130209-90-4P 141196-65-8P

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)

RN 120202-65-5 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, hydrochloride (1:1), (α S)- (CA INDEX NAME)

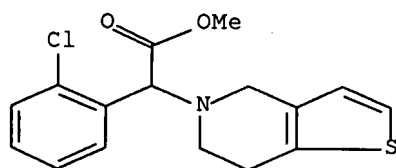
Absolute stereochemistry. Rotation (+).



● HCl

RN 130209-90-4 ZCAPLUS

CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-
dihydro-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 141196-65-8 ZCAPLUS

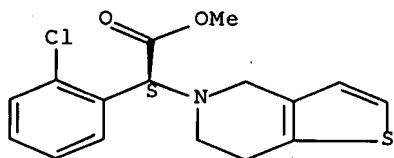
CN Thieno[3,2-c]pyridine-5(4H)-acetic acid, α -(2-chlorophenyl)-6,7-dihydro-, methyl ester, (α S)-, sulfate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 113665-84-2.

CMF C16 H16 Cl N O2 S

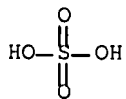
Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9

CMF H2 O4 S



=> d his full

(FILE 'HOME' ENTERED AT 12:54:51 ON 22 MAY 2007)

FILE 'ZCAPLUS' ENTERED AT 12:56:28 ON 22 MAY 2007

```
      E IN2006/APPS
      E IN2006-CH223/APPS
      E IN2006-CHE223/APPS
L1      10 SEA ABB=ON  PLU=ON  ALLA V?/AU
L2      41 SEA ABB=ON  PLU=ON  VYAKARANAM K?/AU
L3      1 SEA ABB=ON  PLU=ON  SIRIGIRI A?/AU
L*** DEL 0 S BODIPATI S?/AU
L4      1 SEA ABB=ON  PLU=ON  BODAPATI S?/AU
L5      8 SEA ABB=ON  PLU=ON  BILLA R?/AU
L*** DEL 0 S GUDIBANDI S?/AU
L7      2 SEA ABB=ON  PLU=ON  ALLA R?/AU
      E GUDIBAN/AU
      E GUDIBANDE S?/AU/AU
L8      13 SEA ABB=ON  PLU=ON  GUDIBANDE S?/AU
L9      1 SEA ABB=ON  PLU=ON  L1 AND (L2 OR L3 OR L4 OR L5 OR L7 OR L8)
L10     1 SEA ABB=ON  PLU=ON  L2 AND (L3 OR L4 OR L5 OR L7 OR L8)
L11     1 SEA ABB=ON  PLU=ON  L3 AND (L4 OR L5 OR L7 OR L8)
L12     1 SEA ABB=ON  PLU=ON  L4 AND (L5 OR L7 OR L8)
L13     0 SEA ABB=ON  PLU=ON  L5 AND (L7 OR L8)
L14     0 SEA ABB=ON  PLU=ON  L7 AND L8
L15     1 SEA ABB=ON  PLU=ON  (L9 OR L10 OR L11 OR L12 OR L13 OR L14)
L16     1 SEA ABB=ON  PLU=ON  L9 AND (L10 OR L11 OR L12 OR L13 OR L14)
      D SCA L15
      D AU
L17     1584 SEA ABB=ON  PLU=ON  CLOP!DOGREL?/BI
L18     0 SEA ABB=ON  PLU=ON  L17 AND (L1 OR L2 OR L3 OR L4 OR L5 OR L7
      OR L8)
```

FILE 'REGISTRY' ENTERED AT 13:11:16 ON 22 MAY 2007

```
      E CLOPEDOGREL/CN
      E CLOPEDOGREL/CN
      E CLOPIDOGREL/CN
L19     10 SEA ABB=ON  PLU=ON  CLOPIDOGREL?/CN
```

FILE 'ZCAPLUS' ENTERED AT 13:12:28 ON 22 MAY 2007

```
L20     1262 SEA ABB=ON  PLU=ON  L19
L21     0 SEA ABB=ON  PLU=ON  L20 AND (L1 OR L2 OR L3 OR L4 OR L5 OR L7
      OR L8)
```

FILE 'REGISTRY' ENTERED AT 13:13:09 ON 22 MAY 2007

```
      E CLOPIDOGREL/CN
L22     1 SEA ABB=ON  PLU=ON  CLOPIDOGREL BISULFATE/CN
```

FILE 'ZCAPLUS' ENTERED AT 13:13:50 ON 22 MAY 2007

```
L23     171 SEA ABB=ON  PLU=ON  L22
L24     47 SEA ABB=ON  PLU=ON  L22/PREP
L25     4406064 SEA ABB=ON  PLU=ON  PREP/RL
L26     47 SEA ABB=ON  PLU=ON  L23 (L) L25
L27     47 SEA ABB=ON  PLU=ON  L22 (L) L25
```

FILE 'REGISTRY' ENTERED AT 13:20:33 ON 22 MAY 2007

```
      D SCA L22
      E METHYL-2-AMINO-2-(2-CHLOROPHENYL)ACETATE/CN
```

E METHYL 2-AMINO-2-(2-CHLOROPHENYL)ACETATE/CN
 E METHYL 2-AMINO-2-(4-CHLOROPHENYL)ACETATE/CN
 E METHYL 2-AMINO-2-(2-CHLOROPHENYL)ACETATE/CN
 L28 0 SEA ABB=ON PLU=ON "METHYL-2-AMINO-2-(4-CHLOROPHENYL)ACETATE"/
 CN
 L29 1 SEA ABB=ON PLU=ON "METHYL 2-AMINO-2-(4-CHLOROPHENYL)ACETATE"/
 CN
 L30 0 SEA ABB=ON PLU=ON "METHYL 2 AMINO 2 (4 CHLOROPHENYL)ACETATE"/
 CN

FILE 'STNGUIDE' ENTERED AT 13:31:12 ON 22 MAY 2007

FILE 'CASREACT' ENTERED AT 13:46:55 ON 22 MAY 2007
 L31 STRUCTURE UPLOADED
 D L31
 L32 0 SEA SSS SAM L31 (0 REACTIONS)

FILE 'ZCAPLUS' ENTERED AT 13:52:06 ON 22 MAY 2007
 L33 1262 SEA ABB=ON PLU=ON L19
 L34 47 SEA ABB=ON PLU=ON L33 AND L27
 D HITSTR 1

FILE 'REGISTRY' ENTERED AT 13:54:22 ON 22 MAY 2007
 E SULFURIC ACID/CN
 L35 1 SEA ABB=ON PLU=ON SULFURIC ACID/CN

FILE 'ZCAPLUS' ENTERED AT 13:54:40 ON 22 MAY 2007
 L36 17 SEA ABB=ON PLU=ON L34 AND L35
 L37 2981503 SEA ABB=ON PLU=ON (RACT OR RGT OR RCT)/RL
 L38 16104 SEA ABB=ON PLU=ON L35 (L) L37
 L39 16 SEA ABB=ON PLU=ON L38 AND L36

FILE 'REGISTRY' ENTERED AT 14:03:10 ON 22 MAY 2007
 L40 STRUCTURE UPLOADED
 L41 19 SEA SSS SAM L40
 L42 426 SEA SSS FUL L40
 SAVE TEMP CHA663STR40L/A L42

FILE 'REGISTRY' ENTERED AT 14:04:06 ON 22 MAY 2007

FILE 'CASREACT' ENTERED AT 14:04:10 ON 22 MAY 2007
 L43 41 SEA ABB=ON PLU=ON L42
 L44 0 SEA SUB=L43 SSS SAM L31 (0 REACTIONS)
 L45 3 SEA SUB=L43 SSS FUL L31 (7 REACTIONS)
 D SCA

FILE 'REGISTRY' ENTERED AT 14:10:54 ON 22 MAY 2007
 L46 STRUCTURE UPLOADED
 L47 STRUCTURE UPLOADED
 L48 9 SEA SUB=L42 SSS SAM L46
 L49 108 SEA SUB=L42 SSS FUL L46
 L50 0 SEA SUB=L42 SSS SAM L47
 L51 13 SEA SUB=L42 SSS FUL L47

FILE 'ZCAPLUS' ENTERED AT 14:14:10 ON 22 MAY 2007
 L52 90 SEA ABB=ON PLU=ON L49 (L) L25
 L53 15 SEA ABB=ON PLU=ON L51 (L) L37
 L54 9 SEA ABB=ON PLU=ON L52 AND L53
 L55 1 SEA ABB=ON PLU=ON L35 AND L54
 L56 15 SEA ABB=ON PLU=ON L51

L57 0 SEA ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5 OR L7 OR L8)
 AND (L39 OR L36 OR L54 OR L55 OR L56)
L58 1371 SEA ABB=ON PLU=ON L42
L59 0 SEA ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5 OR L7 OR L8)
 AND L58

FILE 'REGISTRY' ENTERED AT 14:26:09 ON 22 MAY 2007

FILE 'ZCAPLUS' ENTERED AT 14:26:16 ON 22 MAY 2007

D STAT QUE L39
D STAT QUE L36
D STAT QUE L54
D STAT QUE L55
D STAT QUE L56

L60 31 SEA ABB=ON PLU=ON L39 OR L36 OR (L54 OR L55 OR L56)

FILE 'CASREACT' ENTERED AT 14:27:17 ON 22 MAY 2007

D STAT QUE L45

FILE 'CASREACT, ZCAPLUS' ENTERED AT 14:28:23 ON 22 MAY 2007

L61 31 DUP REM L45 L60 (3 DUPLICATES REMOVED)
 ANSWERS '1-3' FROM FILE CASREACT
 ANSWERS '4-31' FROM FILE ZCAPLUS
 D IBIB ABS CRD L61 1-3
 D IBIB ABS HITIND HITSTR L61 4-31

FILE HOME

FILE ZCAPLUS

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FILE COVERS 1907 - 22 May 2007 VOL 146 ISS 22

FILE LAST UPDATED: 21 May 2007 (20070521/ED)

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FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8

DICTIONARY FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8

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<http://www.cas.org/support/stngen/stndoc/properties.html>

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 18, 2007 (20070518/UP).

FILE CASREACT
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FILE CONTENT:1840 - 19 May 2007 VOL 146 ISS 22

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```
*****
*
*      CASREACT now has more than 12 million reactions
*
*****
```

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> => file registru
'REGISTRU' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'ZCAPLUS'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
```

```
=> file registry
FILE 'REGISTRY' ENTERED AT 14:34:15 ON 22 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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```

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STRUCTURE FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8
DICTIONARY FILE UPDATES: 21 MAY 2007 HIGHEST RN 935505-97-8

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> file zcaplus

FILE 'ZCAPLUS' ENTERED AT 14:34:21 ON 22 MAY 2007

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FILE COVERS 1907 - 22 May 2007 VOL 146 ISS 22

FILE LAST UPDATED: 21 May 2007 (20070521/ED)

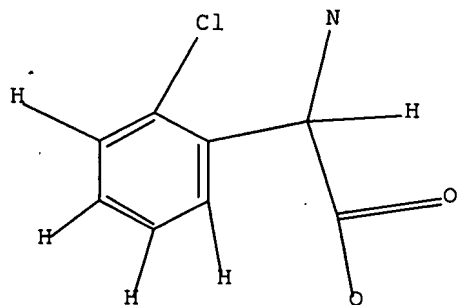
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L66

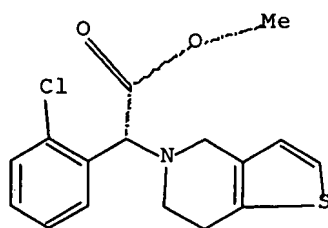
L19	10	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	CLOPIDOGREL?/CN
L22	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	CLOPIDOGREL BISULFATE/CN
L25	4406064	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	PREP/RL
L27	47	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L22 (L) L25
L33	1262	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L19
L34	47	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L33 AND L27
L35	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	SULFURIC ACID/CN
L36	17	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L34 AND L35
L37	2981503	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	(RACT OR RGT OR RCT)/RL
L38	16104	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L35 (L) L37
L39	16	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L38 AND L36
L40			STR			



Structure attributes must be viewed using STN Express query preparation.

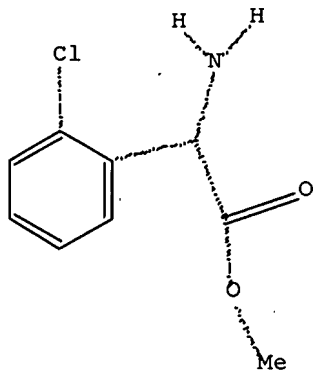
L42 426 SEA FILE=REGISTRY SSS FUL L40

L46 STR



Structure attributes must be viewed using STN Express query preparation.

L47 STR



Structure attributes must be viewed using STN Express query preparation.

L49 108 SEA FILE=REGISTRY SUB=L42 SSS FUL L46

L51 13 SEA FILE=REGISTRY SUB=L42 SSS FUL L47

L52 90 SEA FILE=ZCAPLUS ABB=ON PLU=ON L49 (L) L25

L53 15 SEA FILE=ZCAPLUS ABB=ON PLU=ON L51 (L) L37

L54 9 SEA FILE=ZCAPLUS ABB=ON PLU=ON L52 AND L53

L55 1 SEA FILE=ZCAPLUS ABB=ON PLU=ON L35 AND L54